FIGURE 1

Induction of bone marrow stem cell proliferation

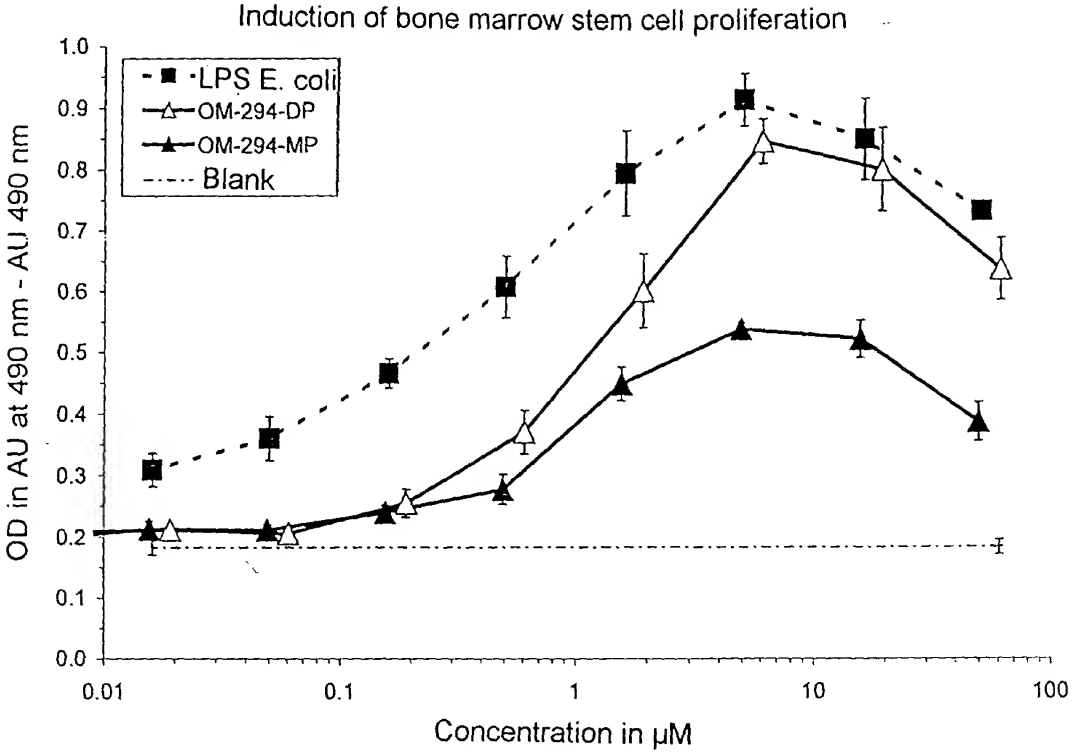


FIGURE 2

Induction of NO production in murine macrophage cells

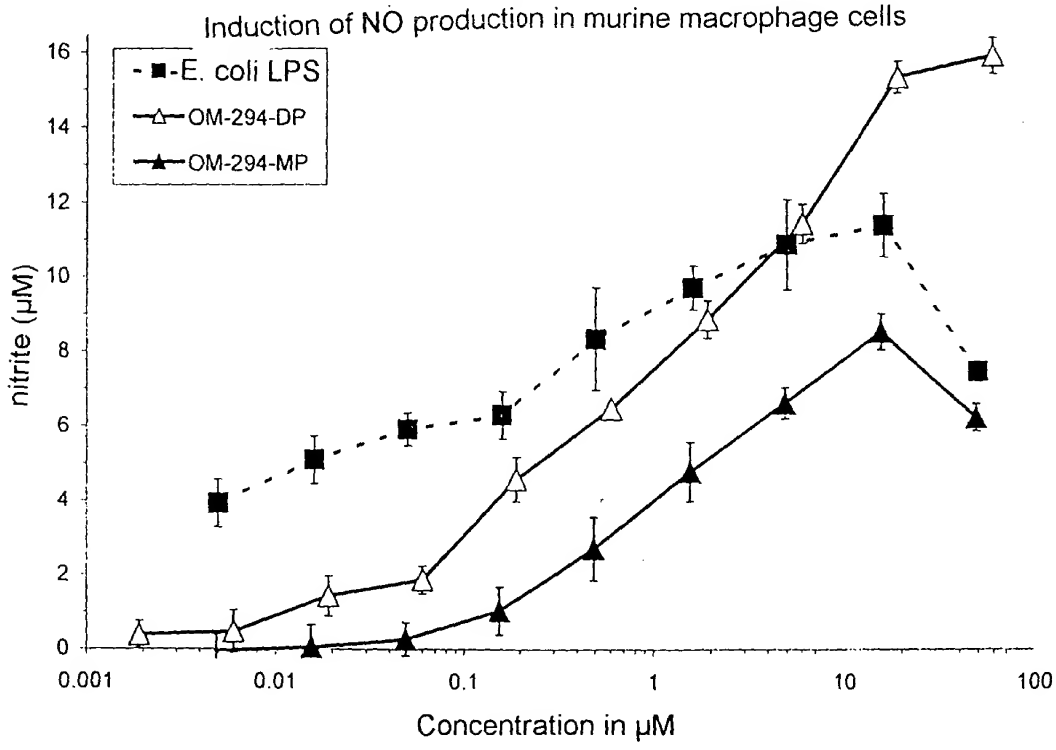


FIGURE 3

Inc › of Dextran-FITC conjugate

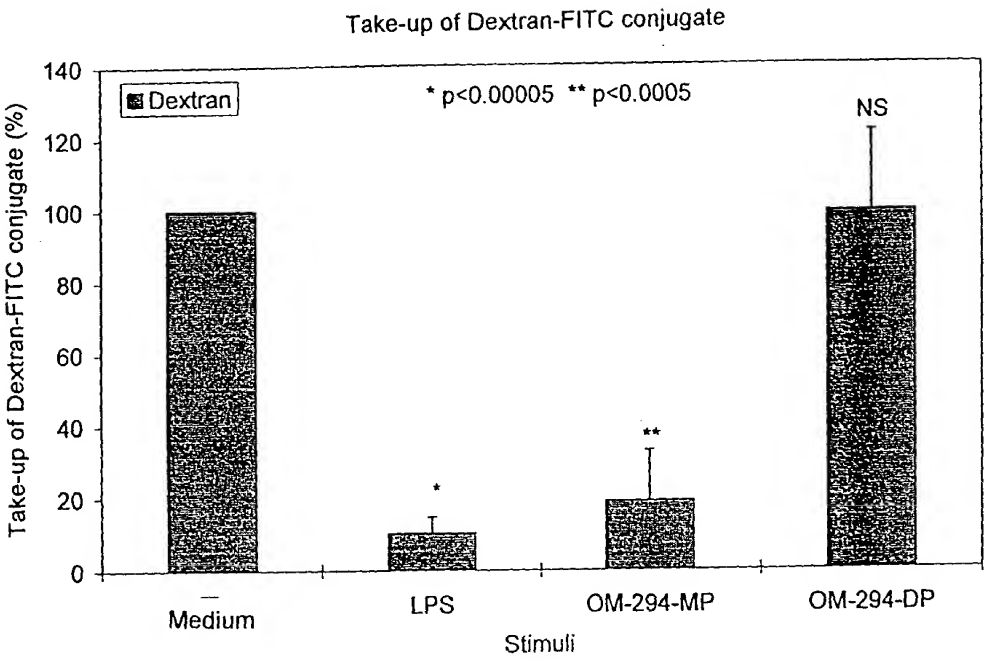


FIGURE 4

Dextran-FITC conjugate take-up : Dose related effect at low concentrations

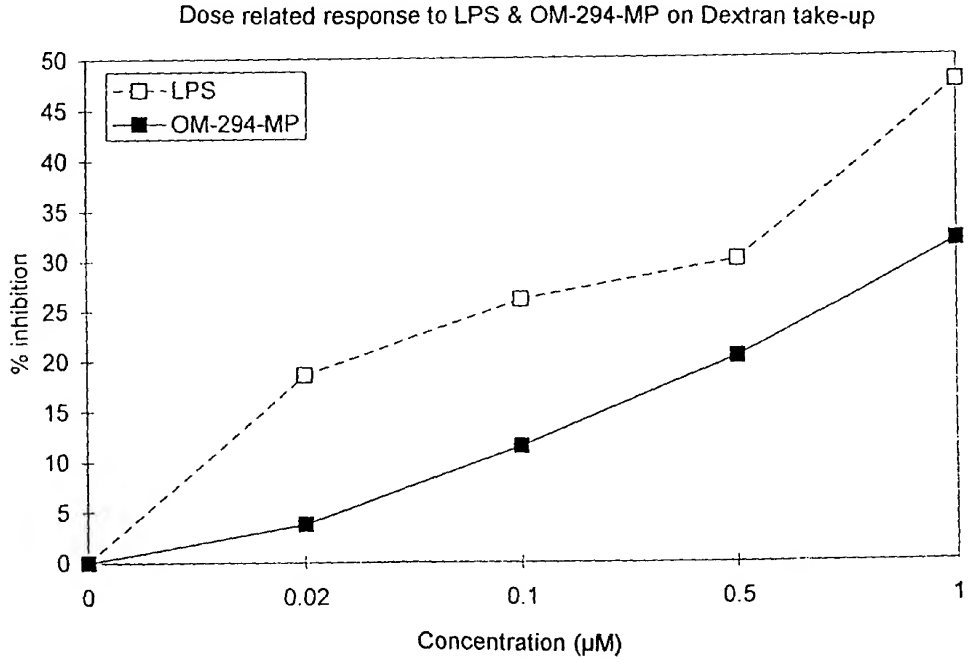


FIGURE 5

Dose related effet in terms of Dextran-FITC conjugate take-up at high concentrations

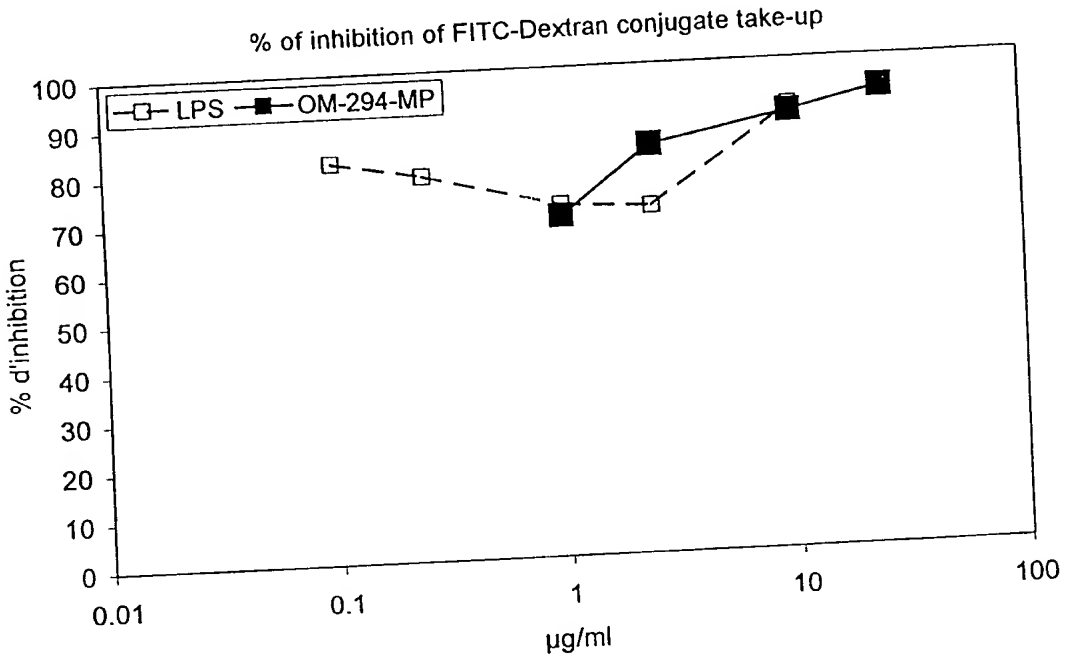


FIGURE 6

CD40 co-stimulating surface marker expression

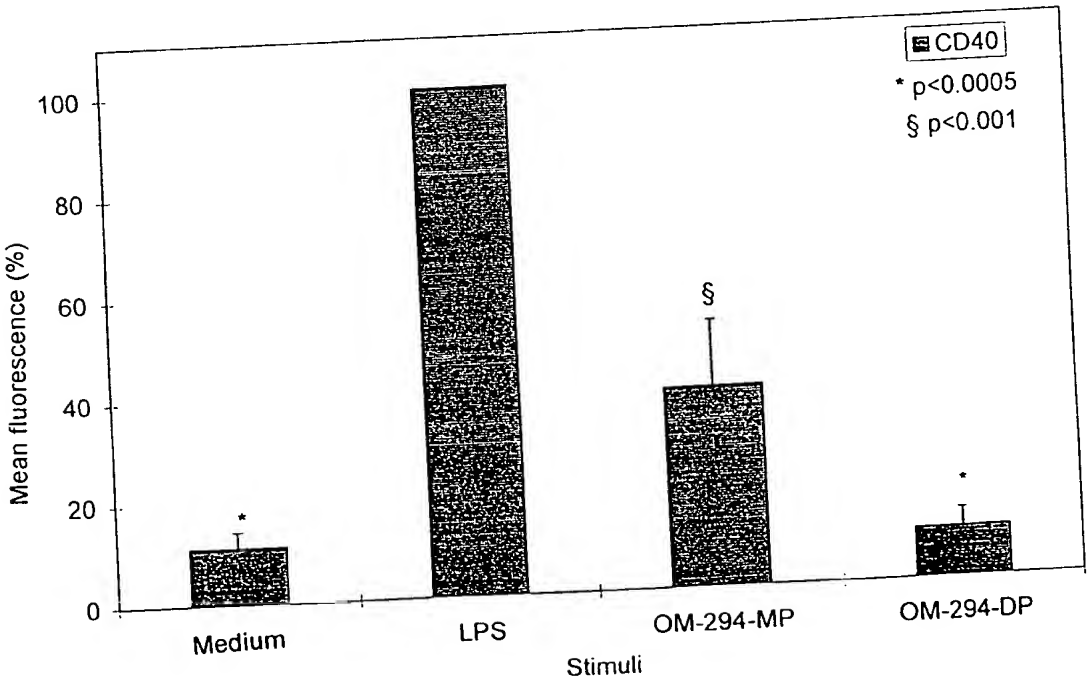


FIGURE 7

Expression of CD86 co-stimulating surface marker

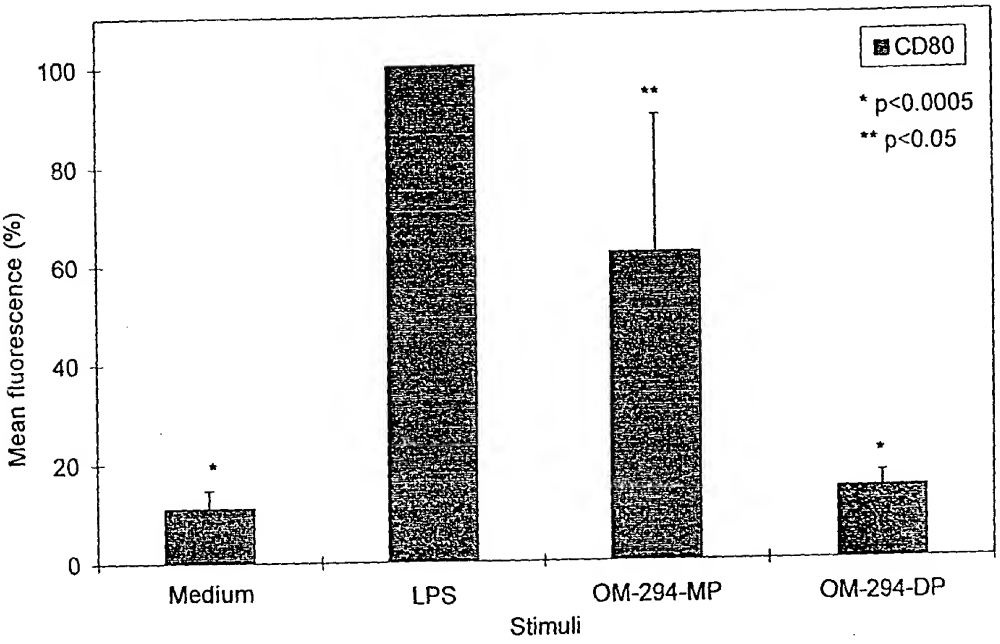


FIGURE 8

Expression of CD83 co-stimulating surface marker

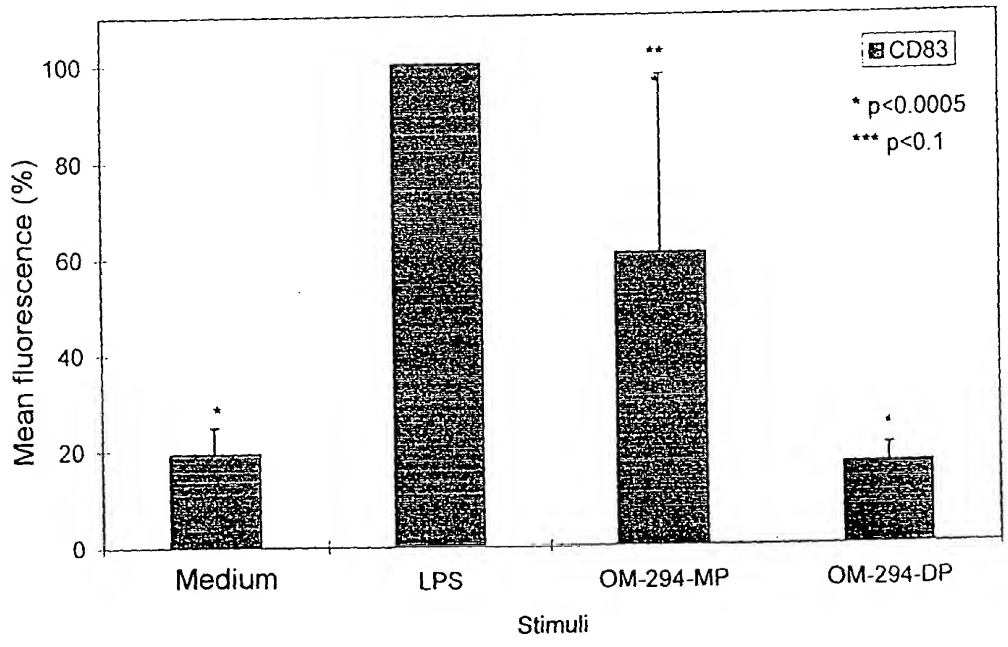


FIGURE 9

Expression of CD80 co-stimulating surface marker

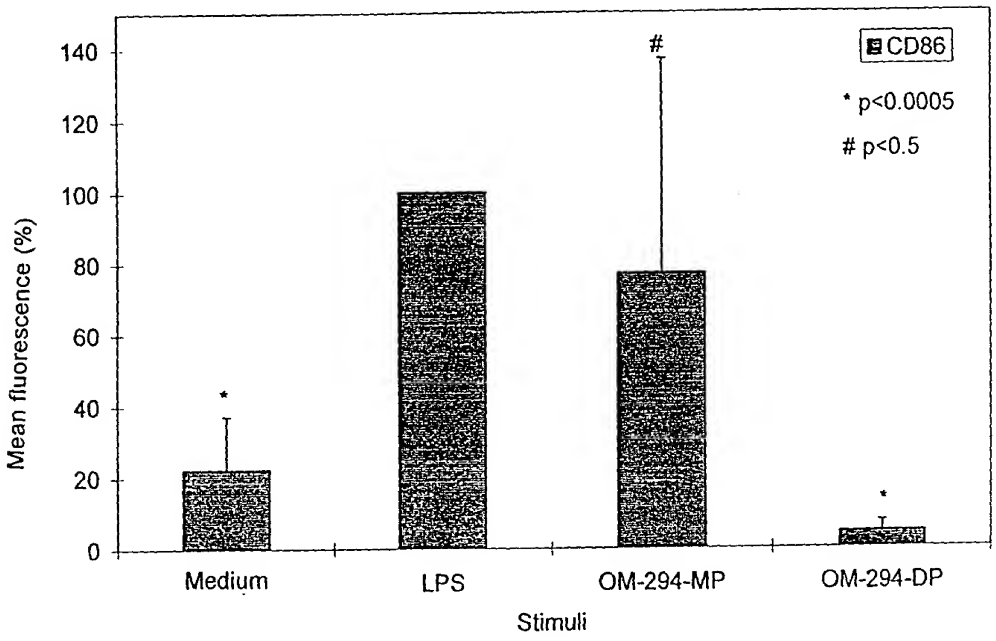


FIGURE 10

Effect of OM-294-MP and OM-294-DP products on α TNF production by predendritic cells at DC-6 stage

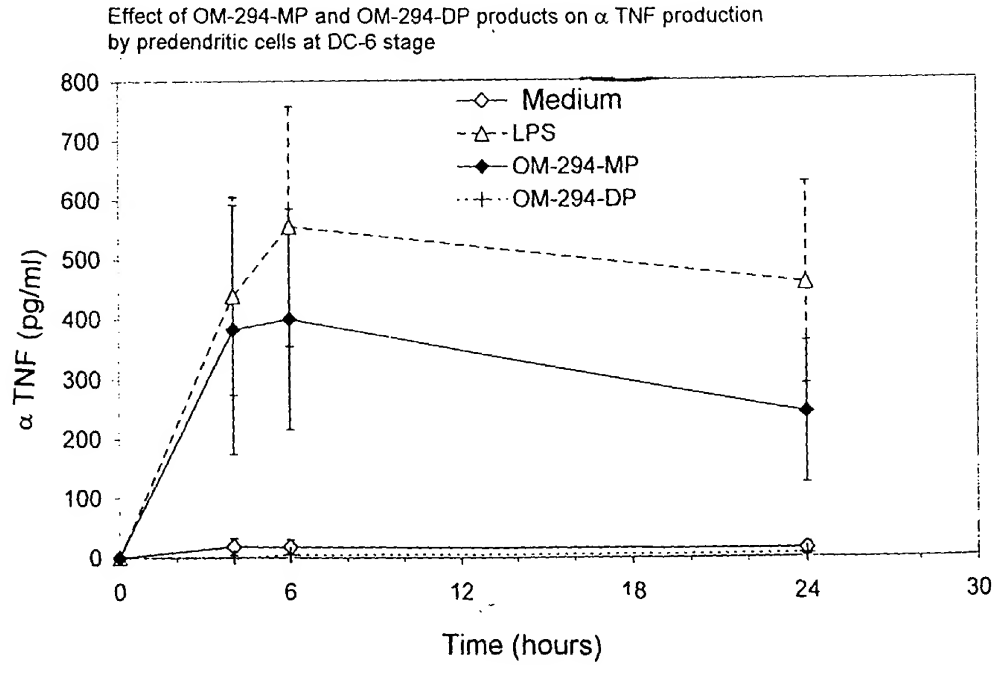


FIGURE 11

Effect of OM-294-MP and OM-294-DP products on IL-12 p70 production by predendritic cells at DC-6 stage (IFN = γ IFN)

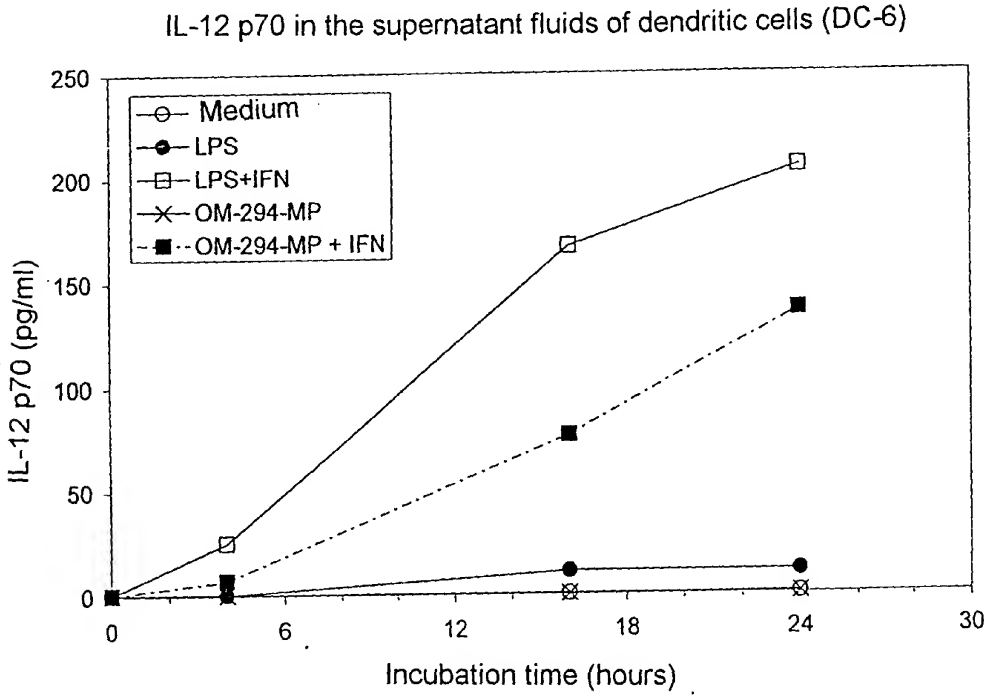


FIGURE 12

Effect of OM-294-MP products on IL-12 p70 production by monocytes

(IFN = γ IFN)

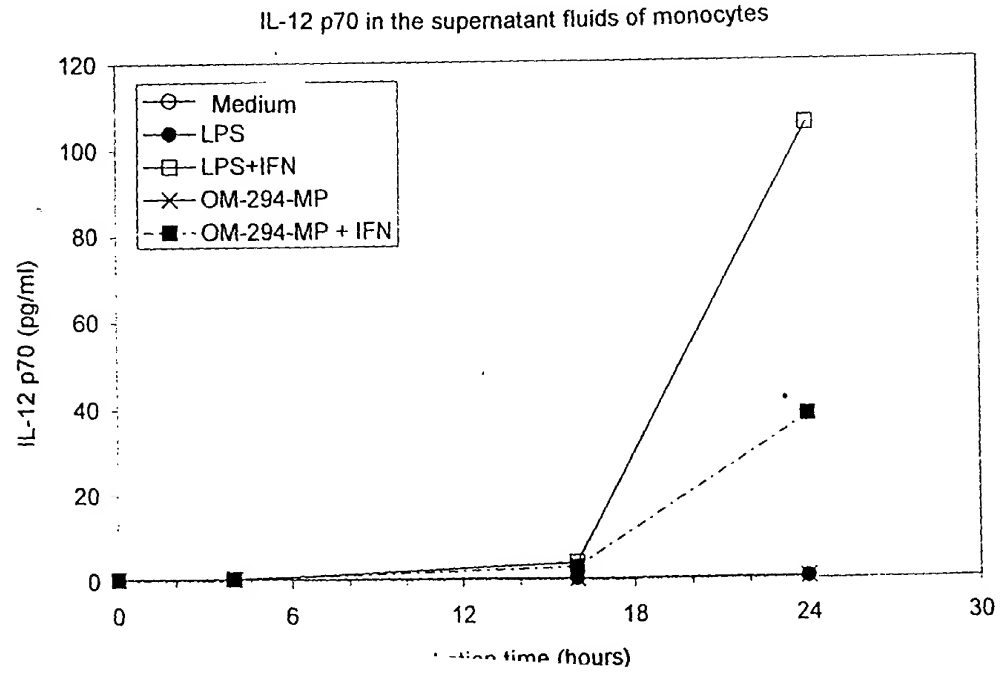


FIGURE 13

ELISA 2 after the first immunization treatment

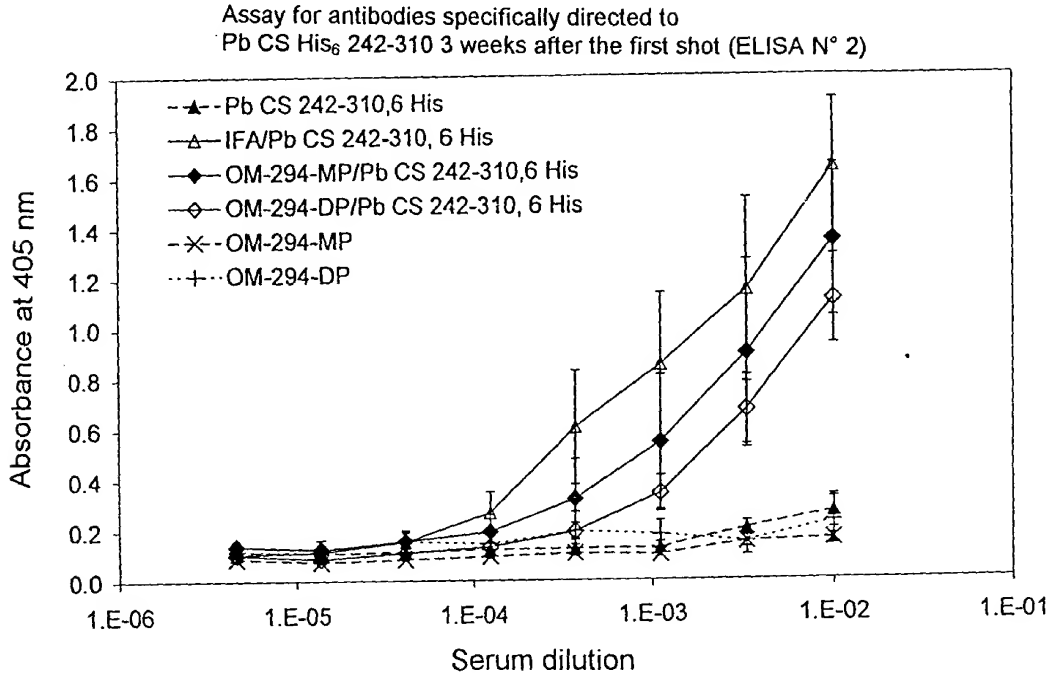


FIGURE 14

ELISA 3 after the second immunization treatment

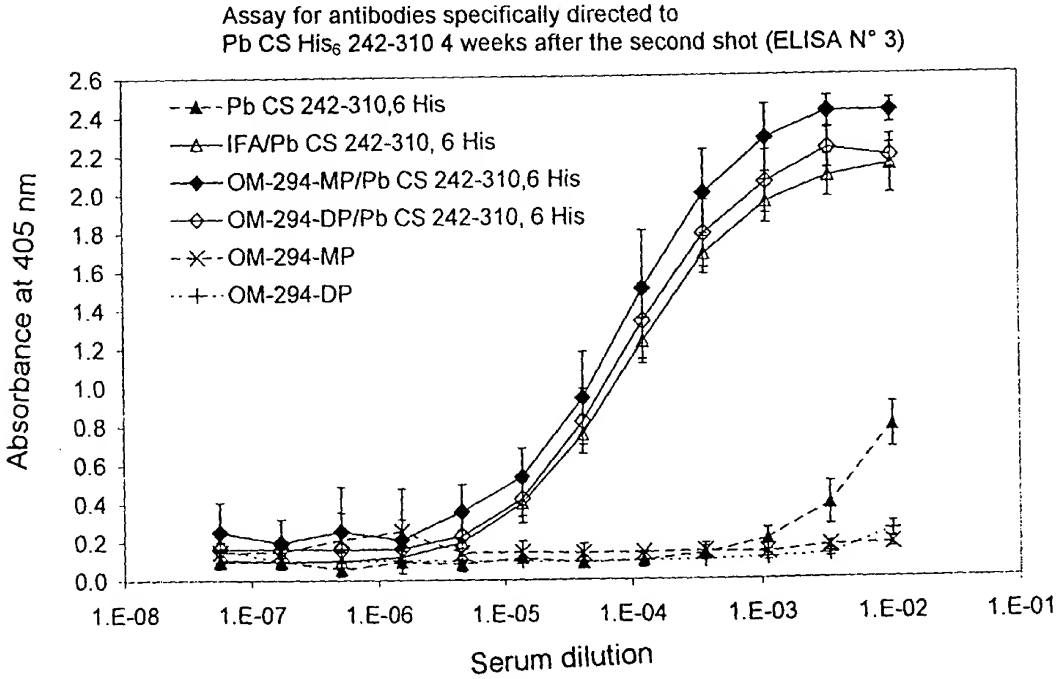


FIGURE 15

ELISA 4 after the third immunization treatment

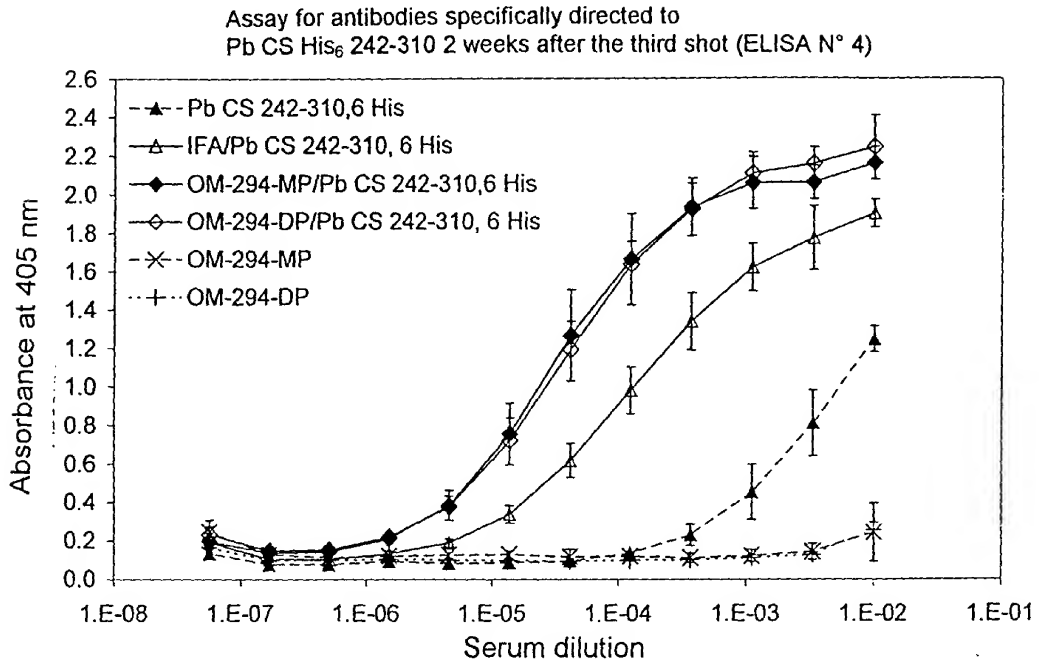


FIGURE 16

Antibody titer before and after one, two and three immunizations treatments

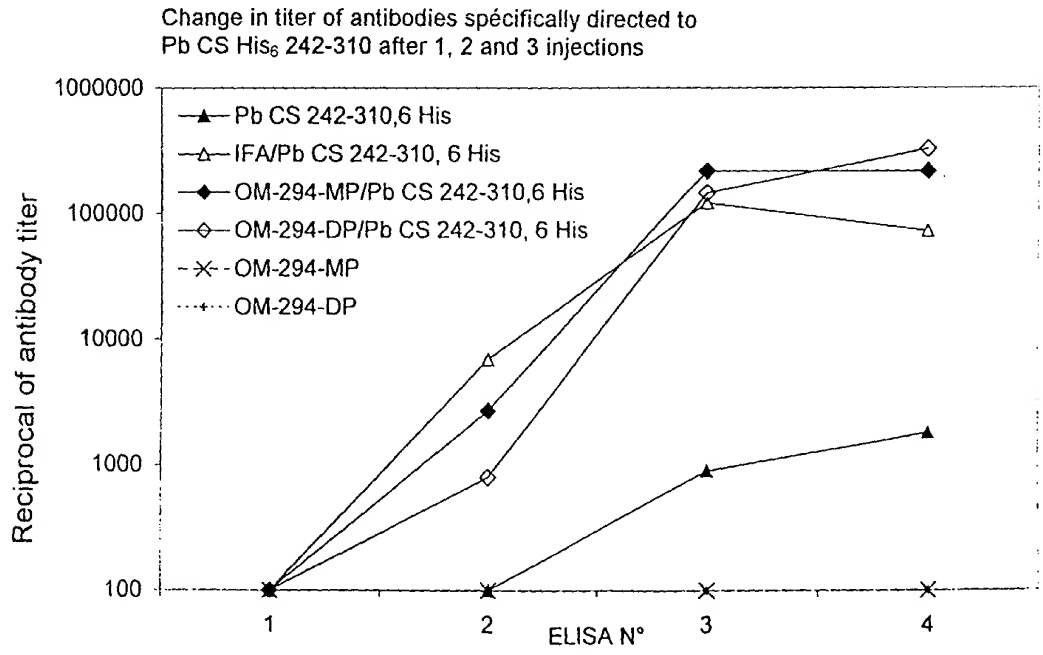


FIGURE 17

ELISPOT γ IFN-producing lymphocytes of inguinal lymph nodes stimulated by Pb CS 245 - 252 one week after the second immunization treatment

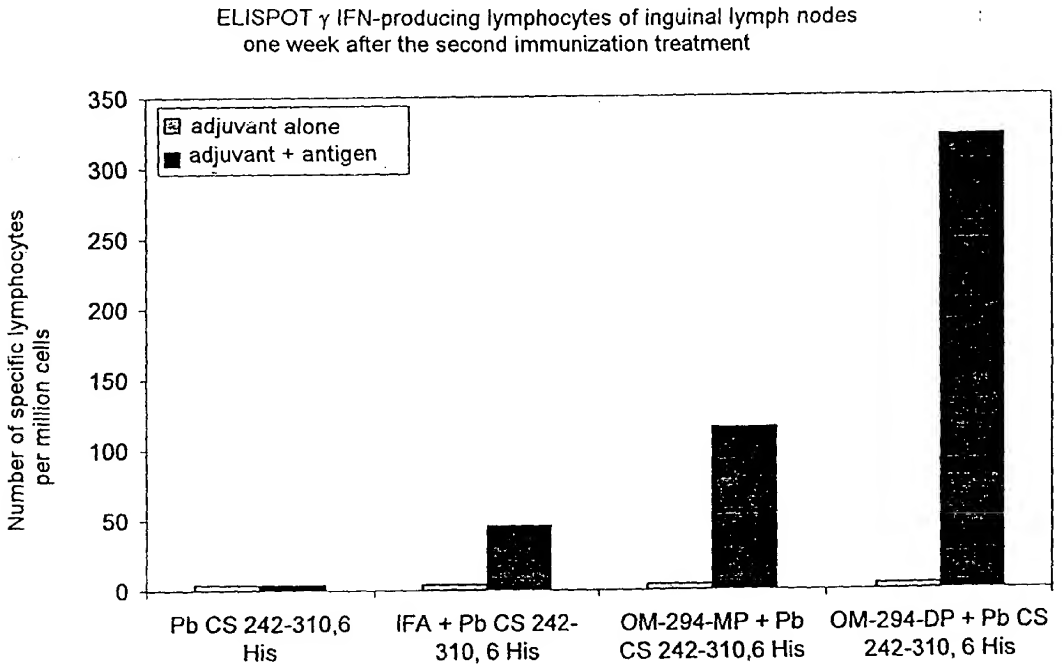


FIGURE 18

ELISPOT γ IFN-producing lymphocytes of the spleen stimulated by Pb CS 245 - 252 one week after the second immunization

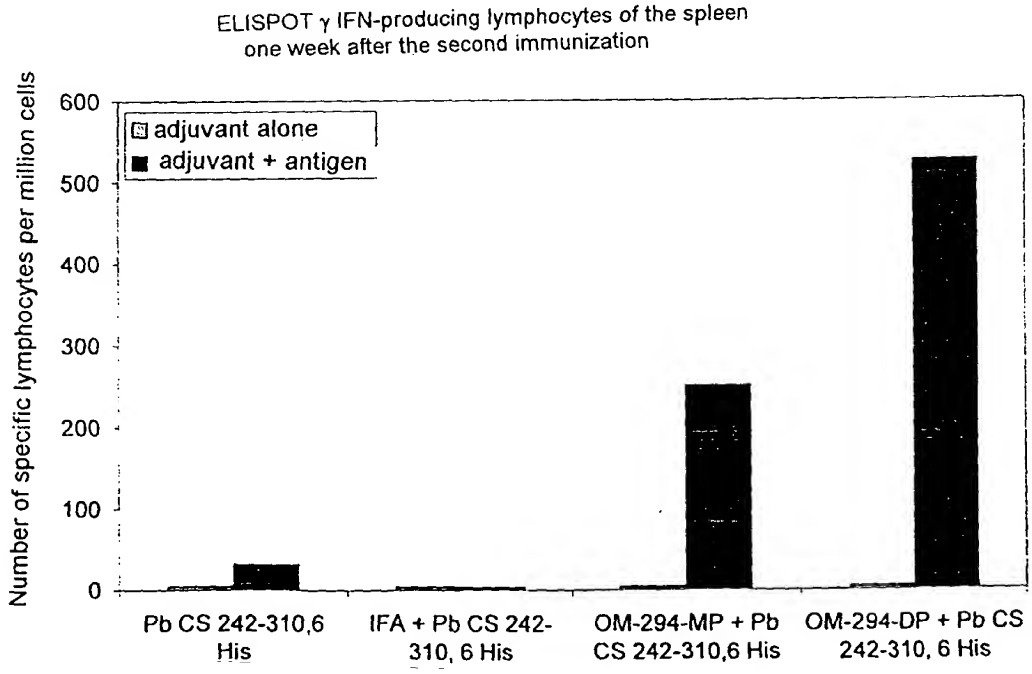


FIGURE 19

ELISPOT γ IFN-producing lymphocytes of the spleen stimulated by Pb CS 245 - 252 one week after the second immunization

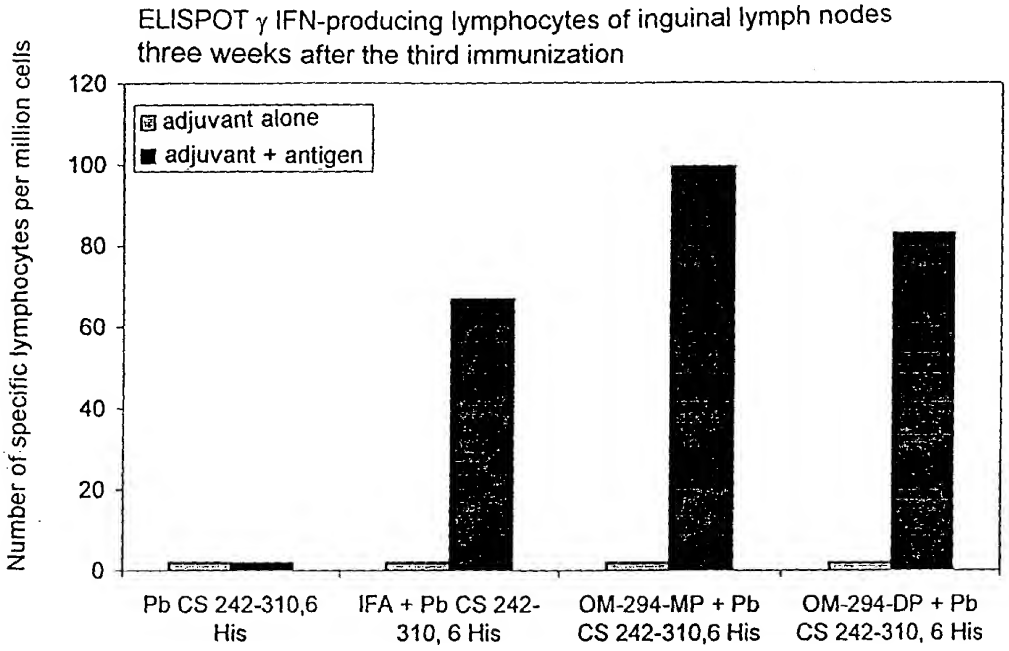


FIGURE 20

ELISPOT γ IFN-producing lymphocytes of the spleen stimulated by Pb CS 245 - 252 three weeks after the third immunization

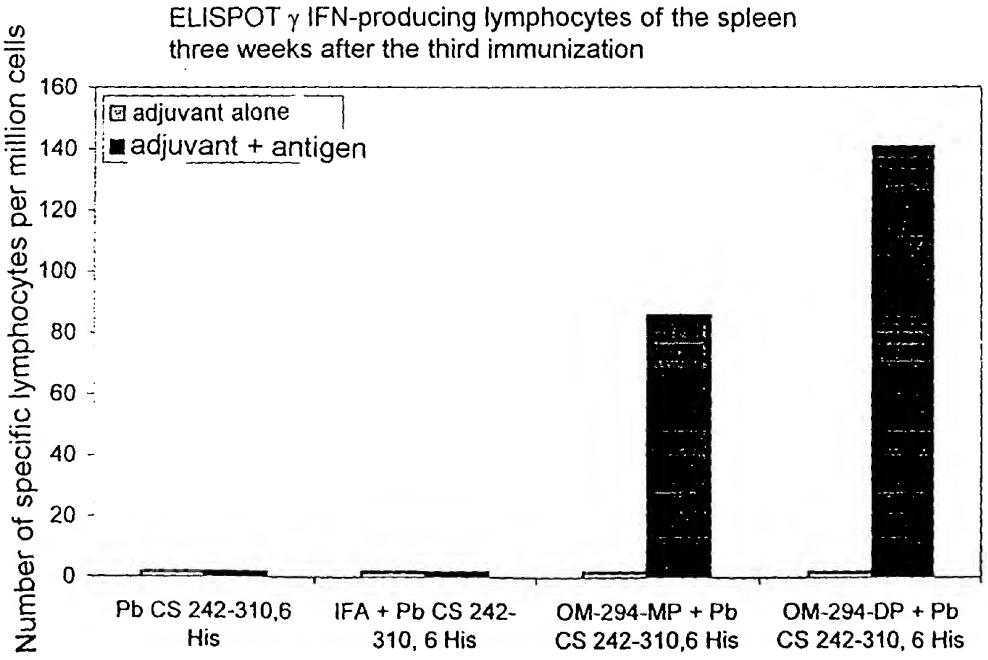


FIGURE 21

Electrophoretogram of OM-294-DP alone, of Pb CS His6-242-310 antigen alone and of Pb CS His6-242-310 - OM-294-DP complex

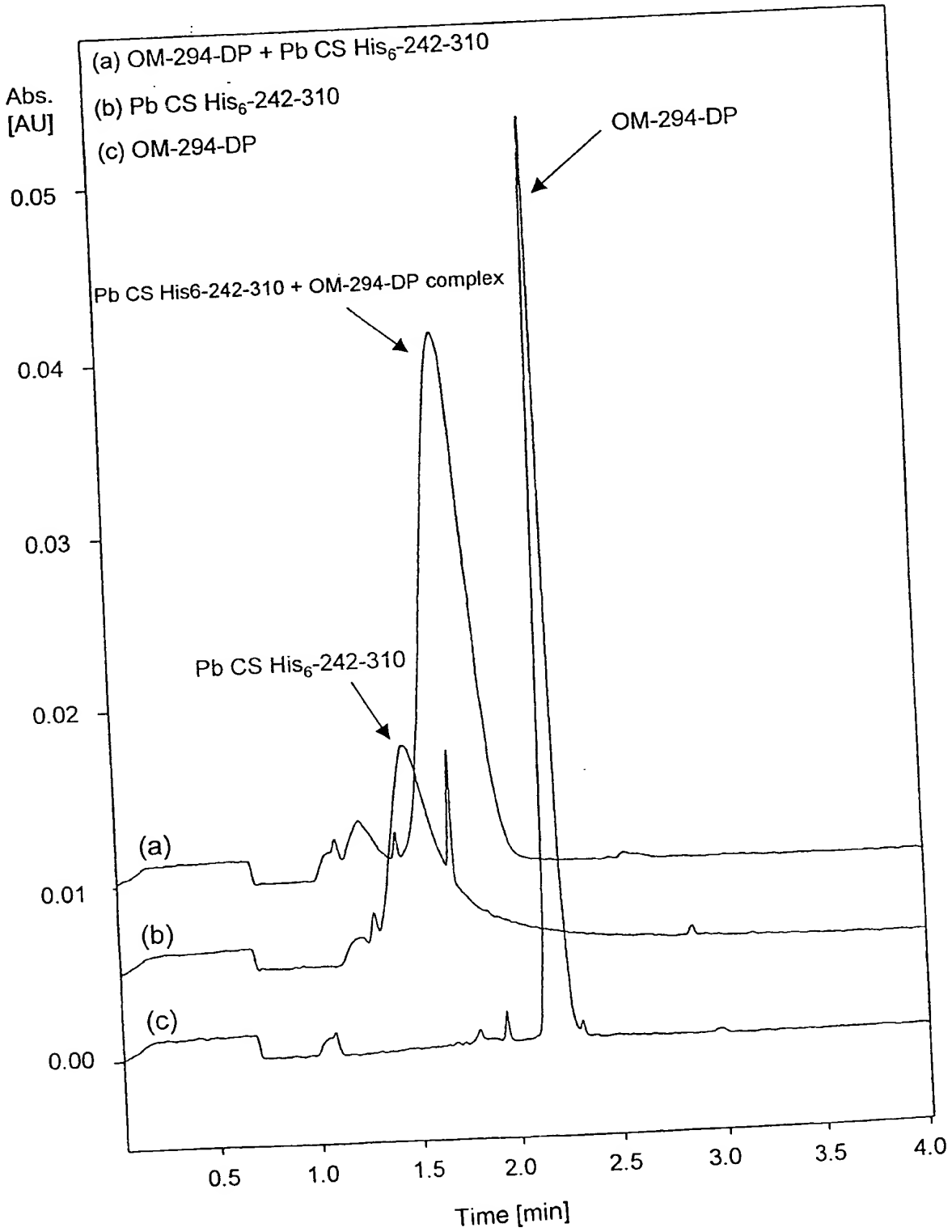


FIGURE 22

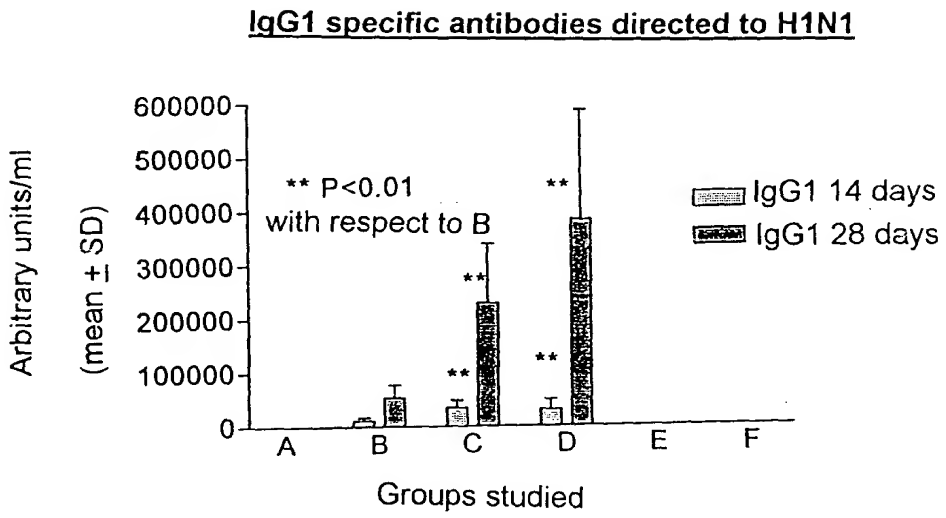


FIGURE 23

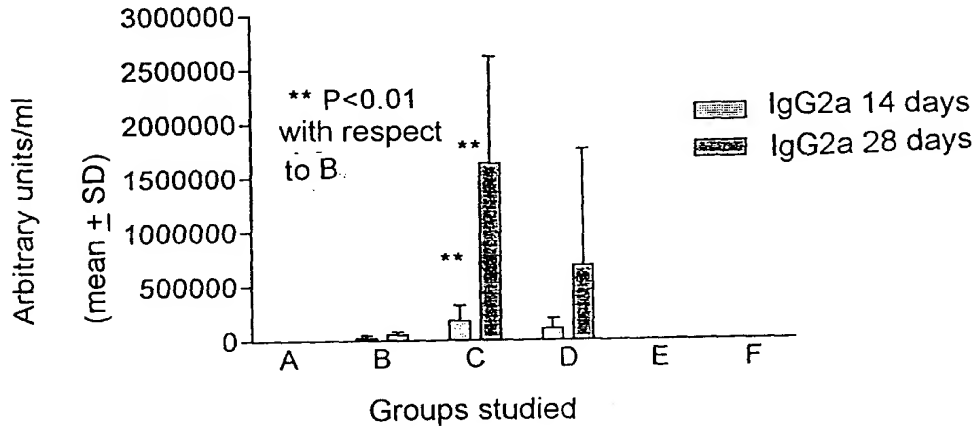


FIGURE 24

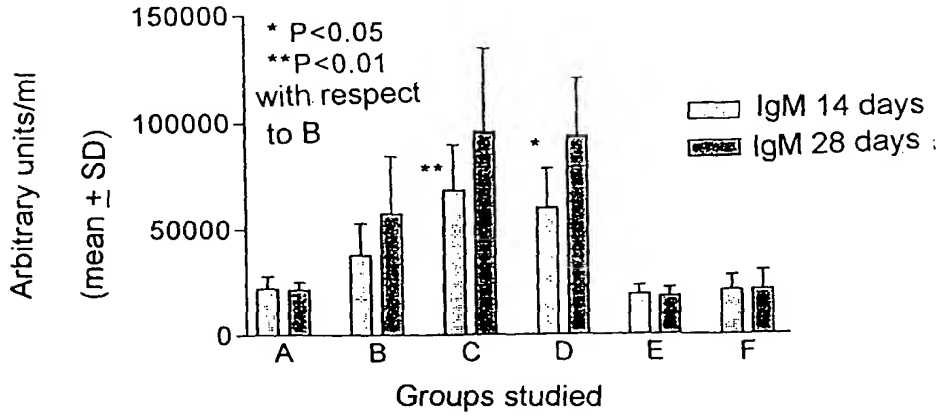


FIGURE 25

IgG1 specific antibodies directed to ovalbumin

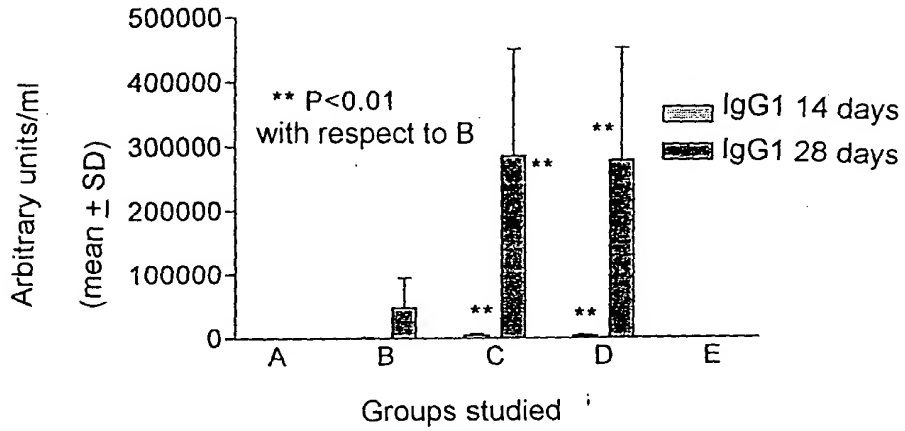


FIGURE 26

IgG2a specific antibodies directed to ovalbumin

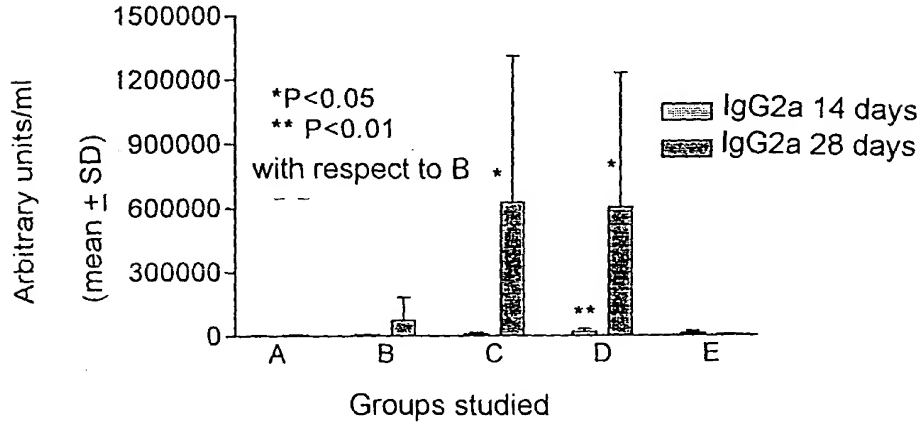


FIGURE 27

IgM specific antibodies directed to ovalbumin

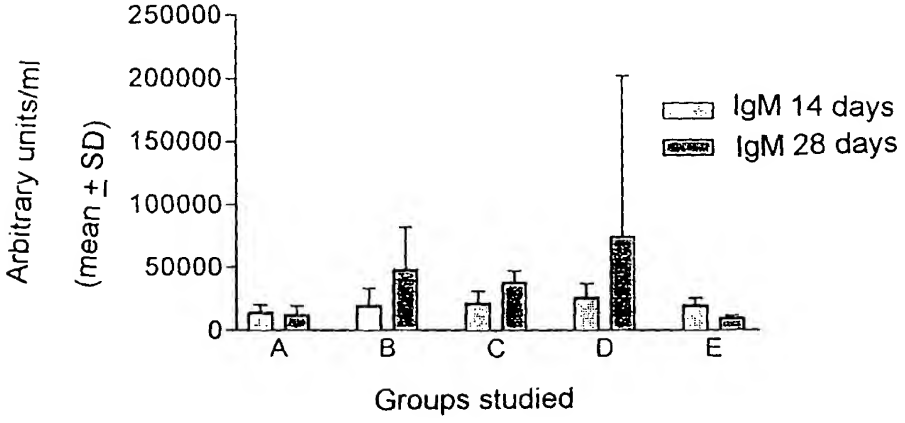


FIGURE 28

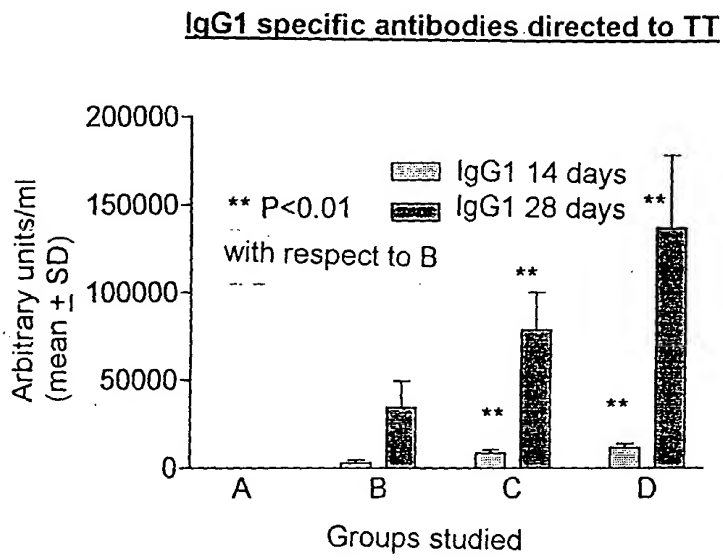


FIGURE 29

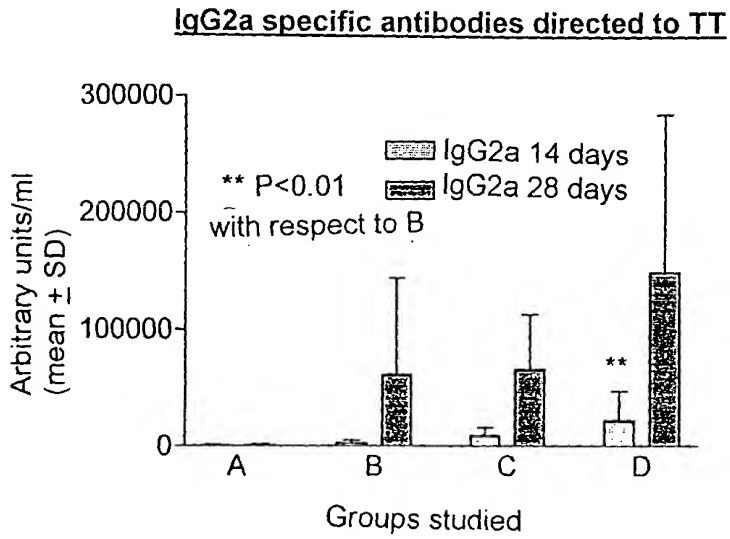


FIGURE 30 (a)

Increase in the anti-gp63 immune response under the effect of OM-294-MP adjuvant : Comparison with BCG

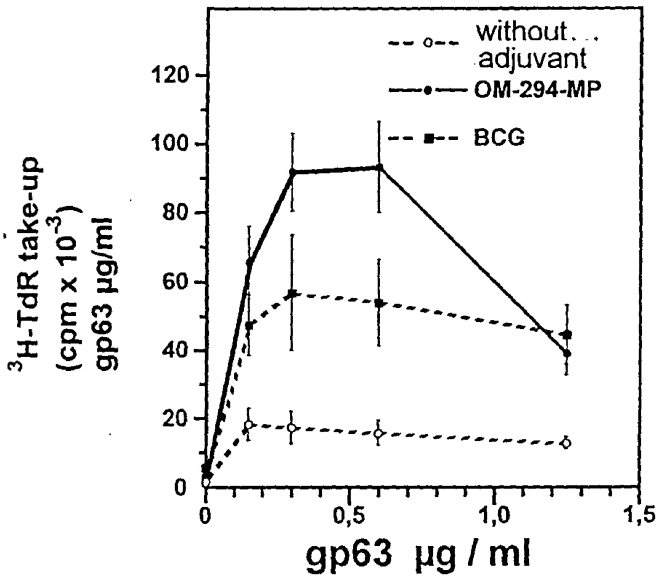


FIGURE 30 (b)

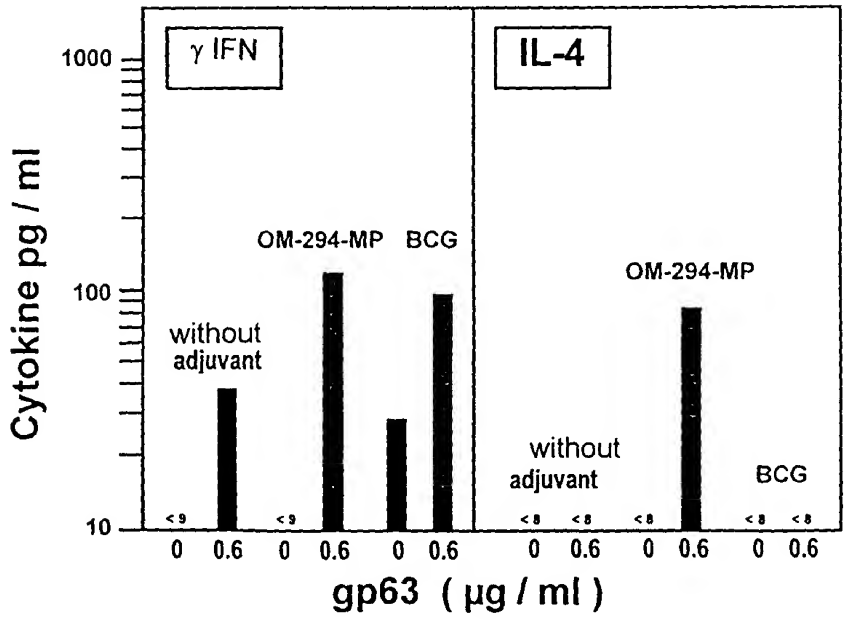


FIGURE 31 (a)

In vitro lymph node lymphocyte response derived from mice previously immunized in vivo with LmCPb antigen : effect of OM-294-MP adjuvant during the primary response

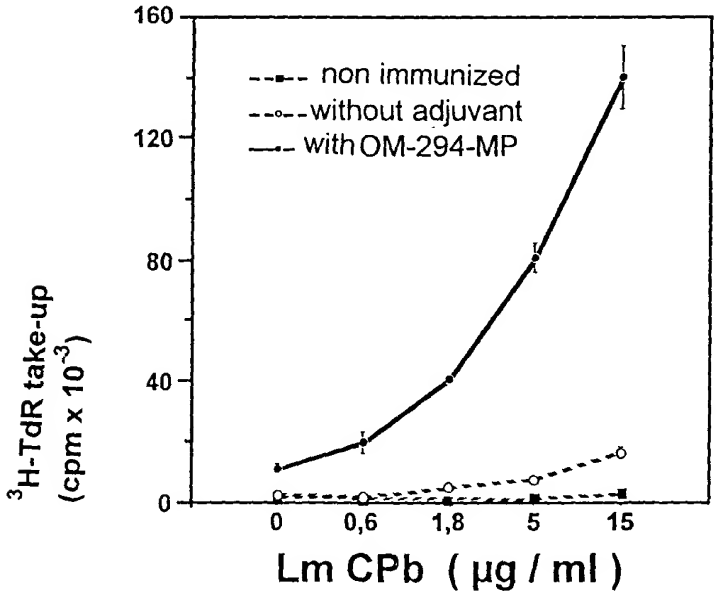


FIGURE 31 (b)

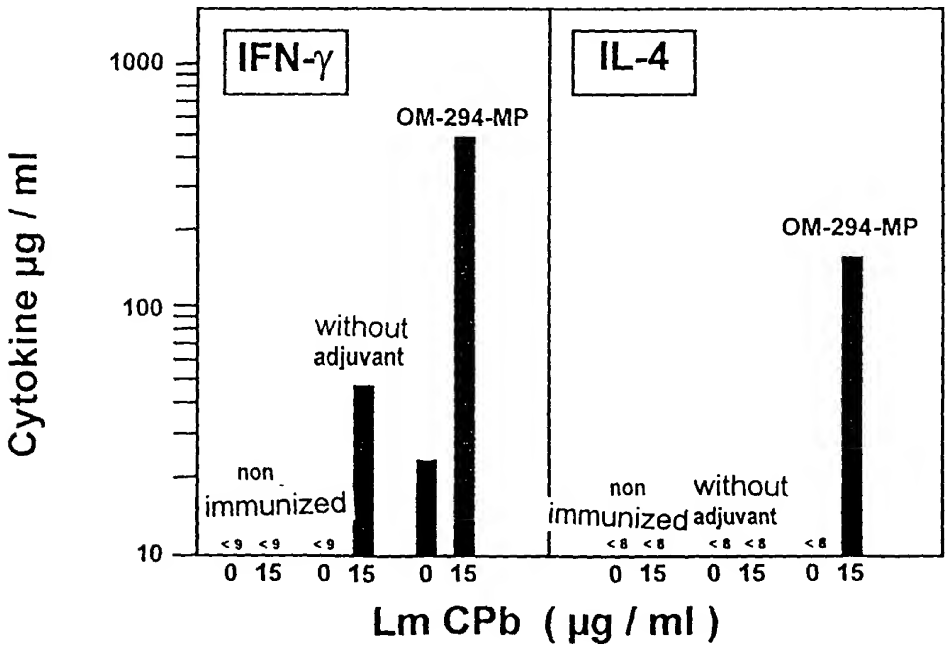


FIGURE 32 (a)

Increase in the anti-LmCPb immune response under the effect of OM-294-MP adjuvant : Comparison with BCG

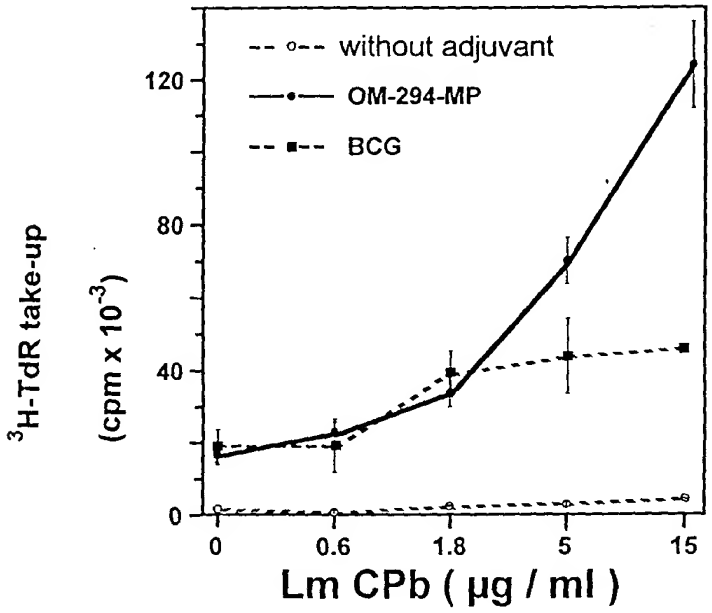
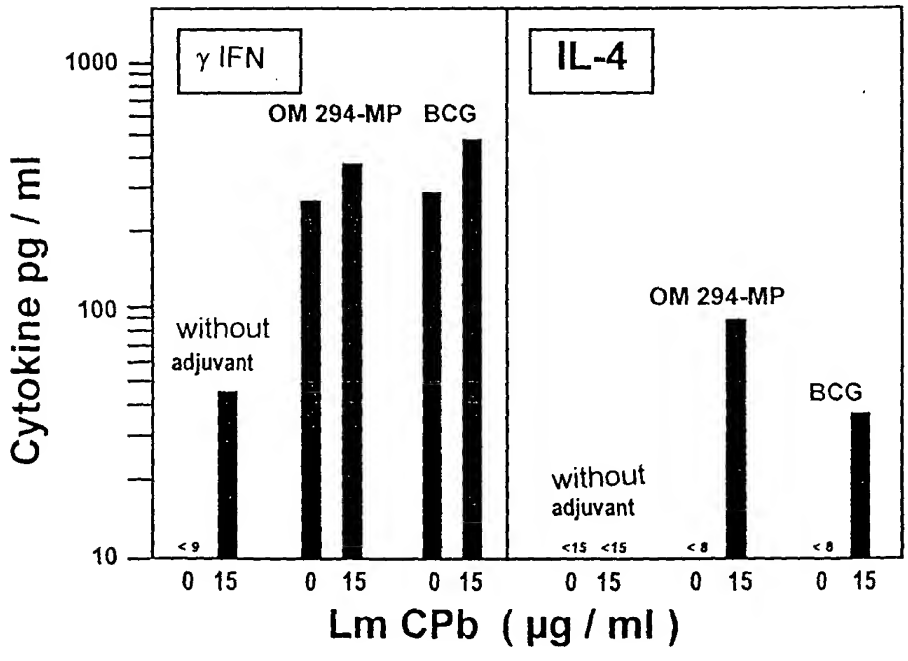


FIGURE 32 (b)



YNTHESIS SCHEME 1

Bn = benzyl
Boc = t-butyloxycarbonyl
Ph = phenyl

Z = benzyloxycarbonyl
R = allyl
Y = protecting group

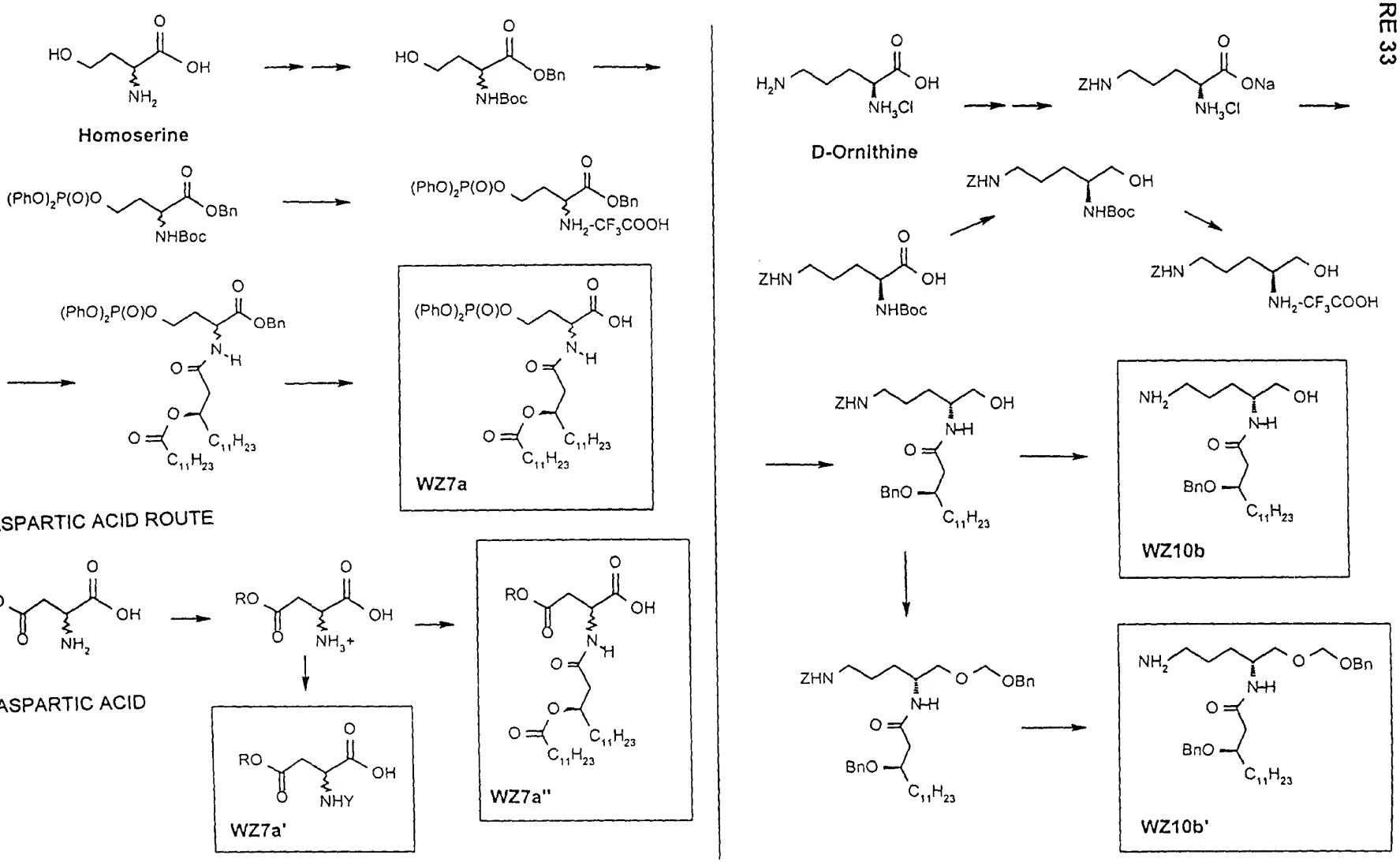


FIGURE 34

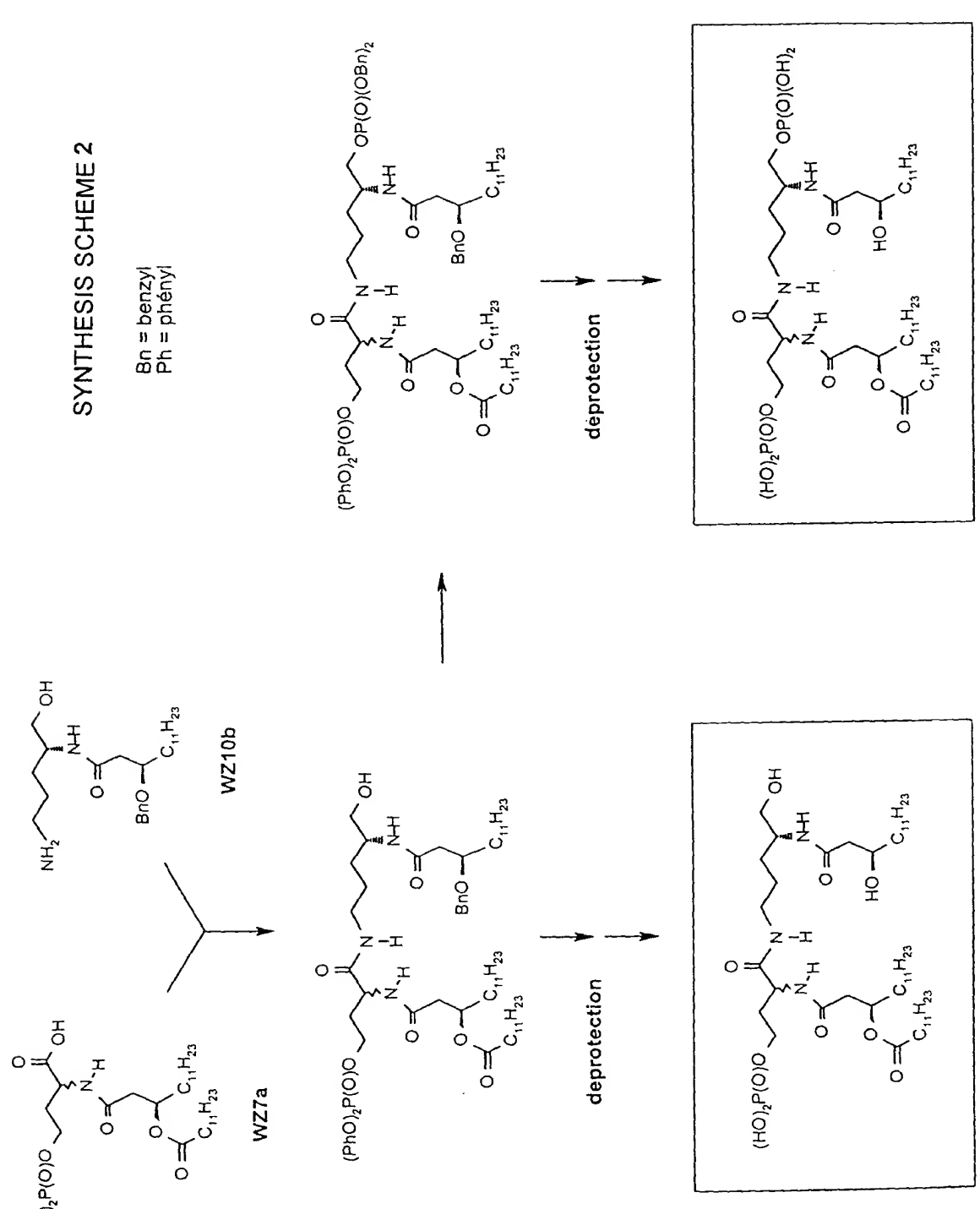

SYNTHESIS SCHEME 2
Bn = benzyl
Ph = phényl
WZ10b
WZ7a
deprotection
deprotection

FIGURE 35

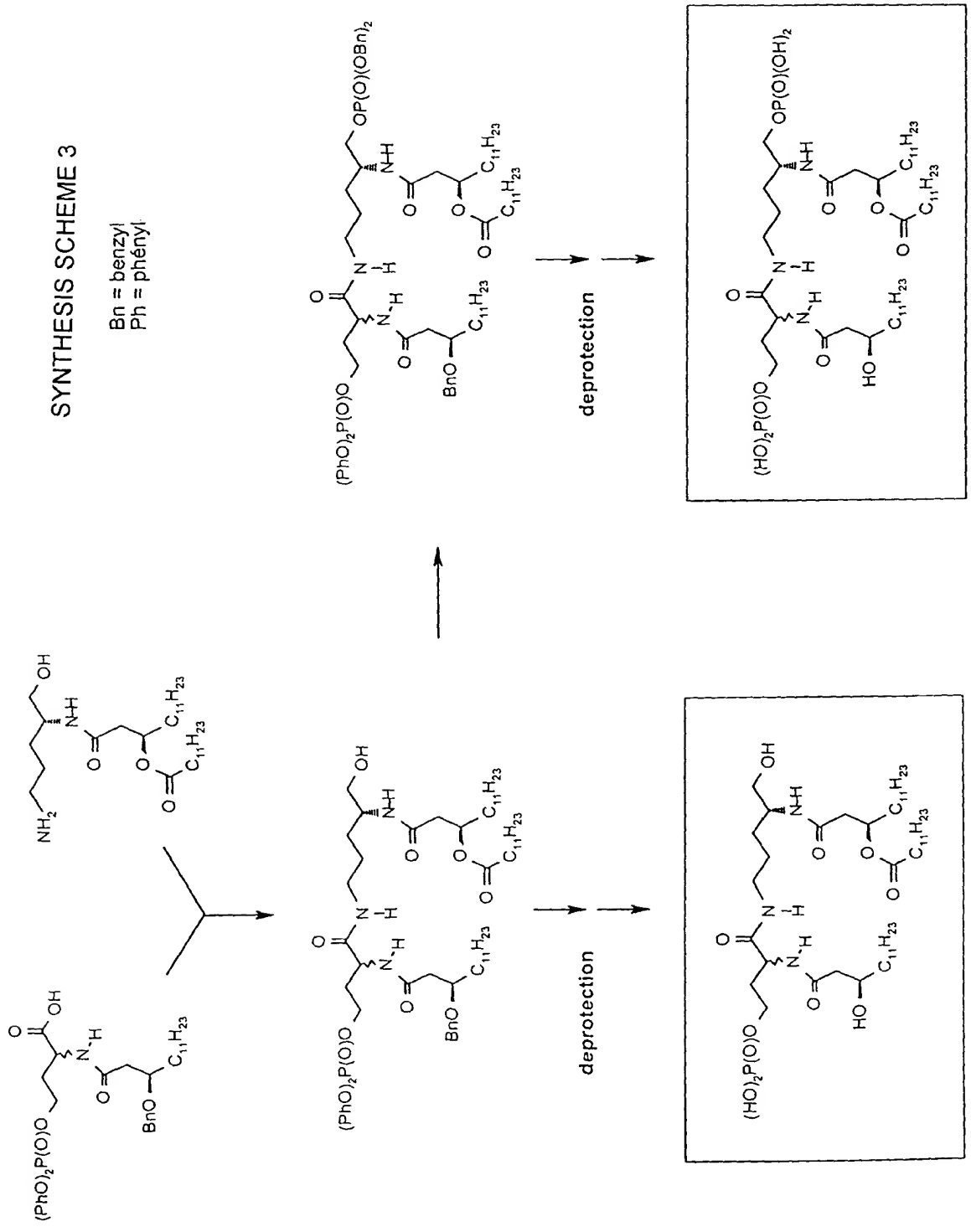

SYNTHESIS SCHEME 3
Bn = benzyl
Ph = phényl
deprotection
deprotection

FIGURE 36

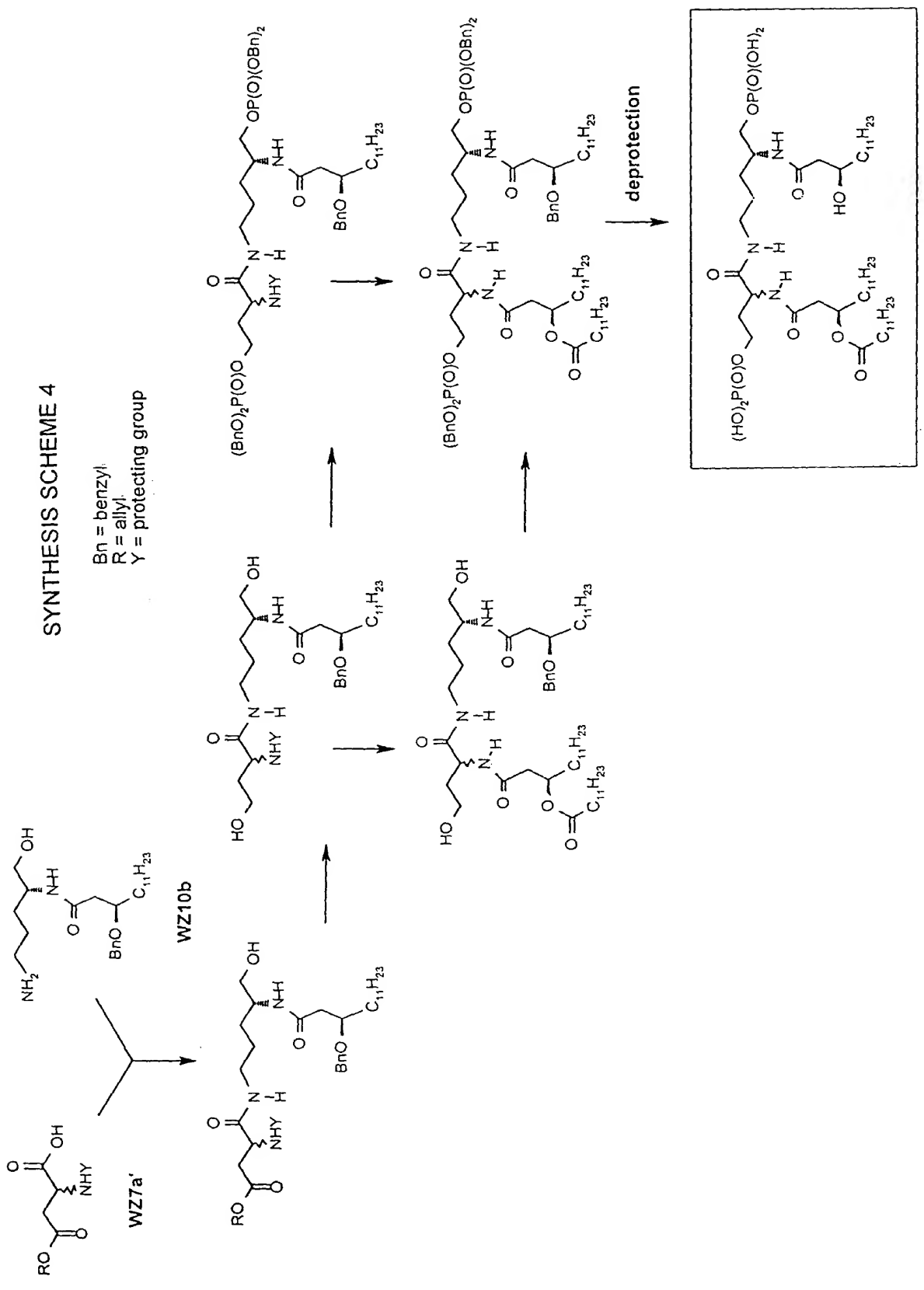

SYNTHESIS SCHEME 4
Bn = benzyl
R = allyl
Y = protecting group
WZ7a'
WZ10b
deprotection

FIGURE 37

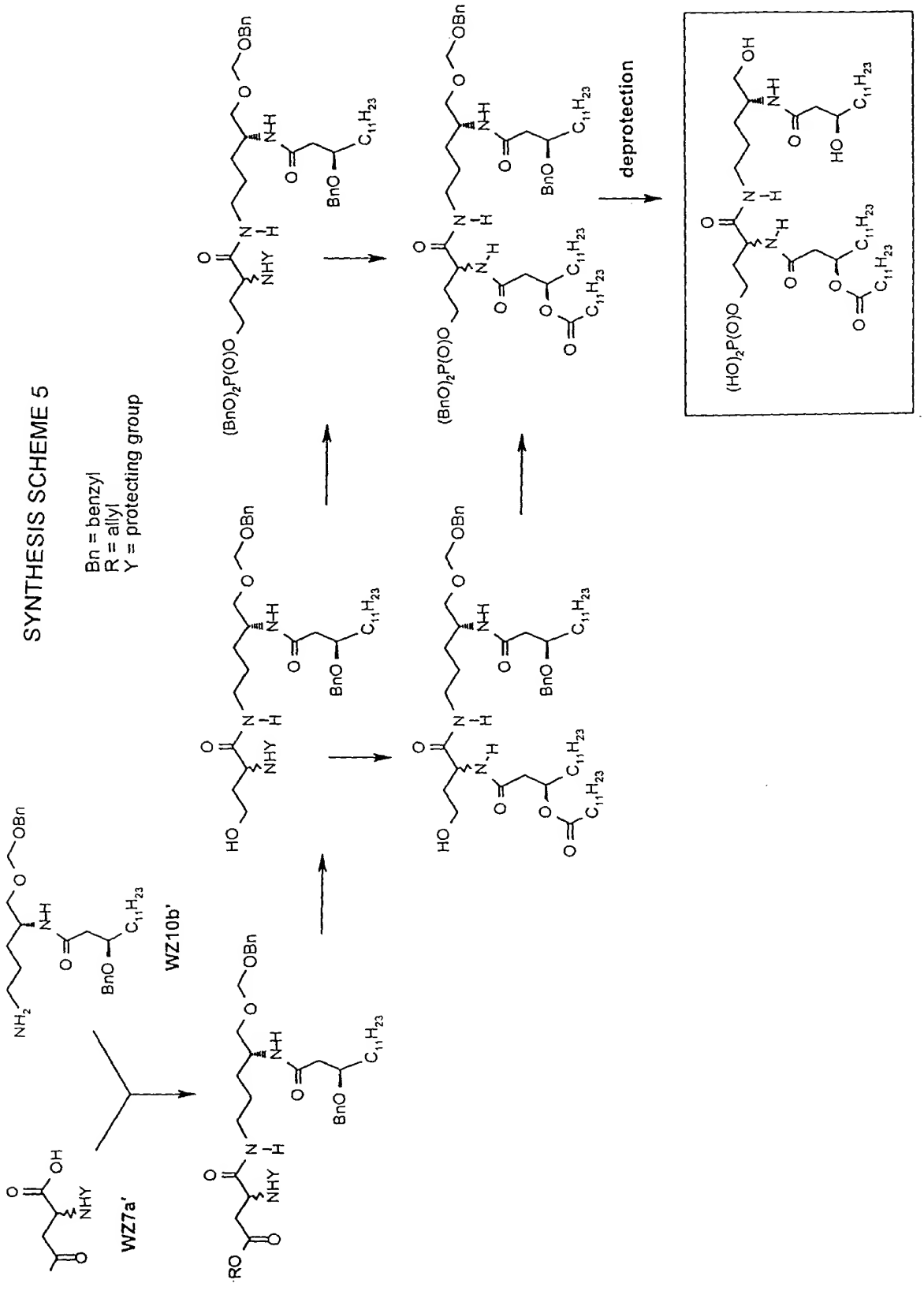

SYNTHESIS SCHEME 5
Bn = benzyl
R = allyl
Y = protecting group
WZ7a'
WZ10b'
deprotection

FIGURE 38

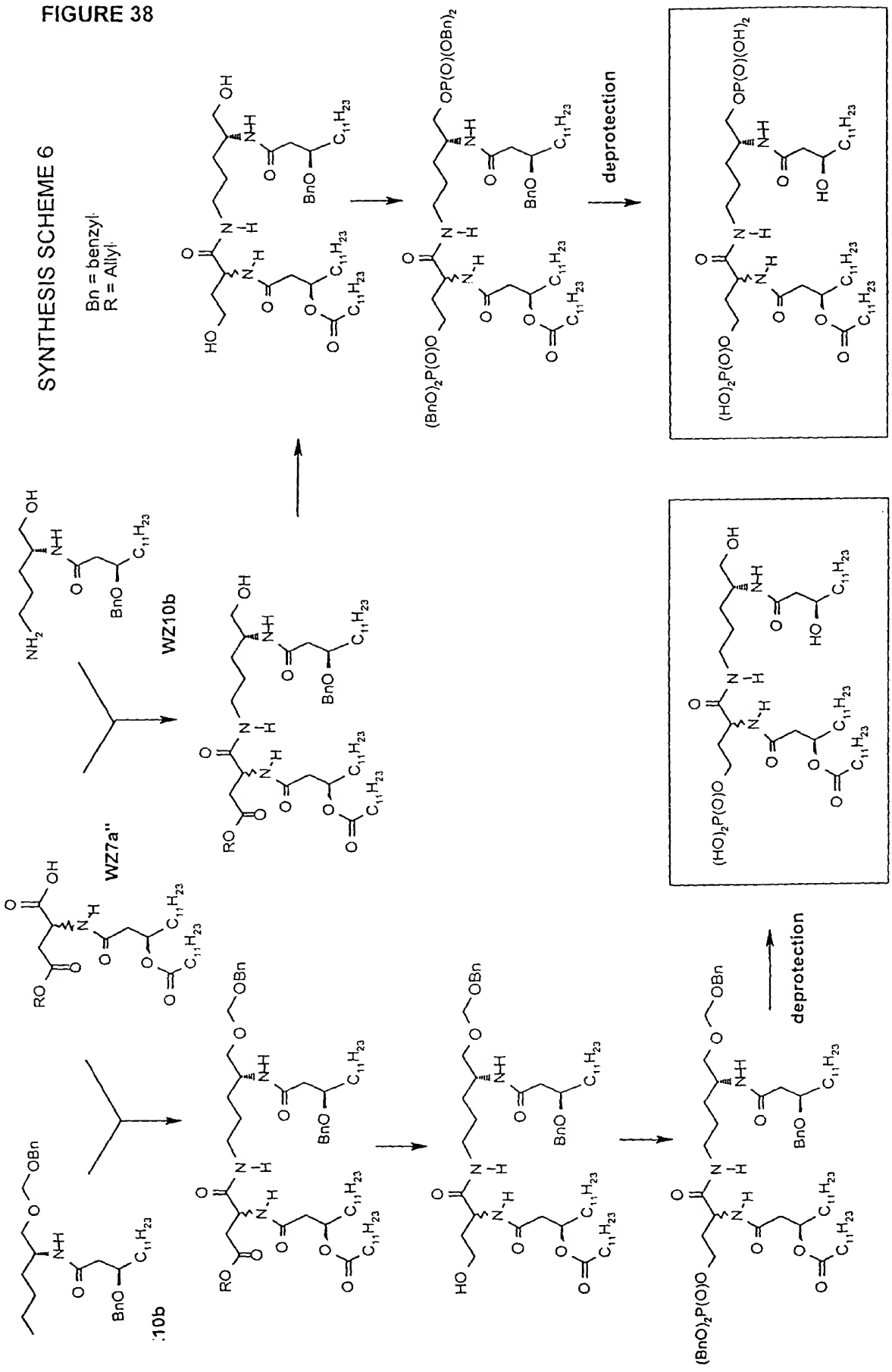

SYNTHESIS SCHEME 6
Bn = benzyl
R = Allyl
WZ10b
WZ7a''
deprotection
deprotection

FIGURE 39

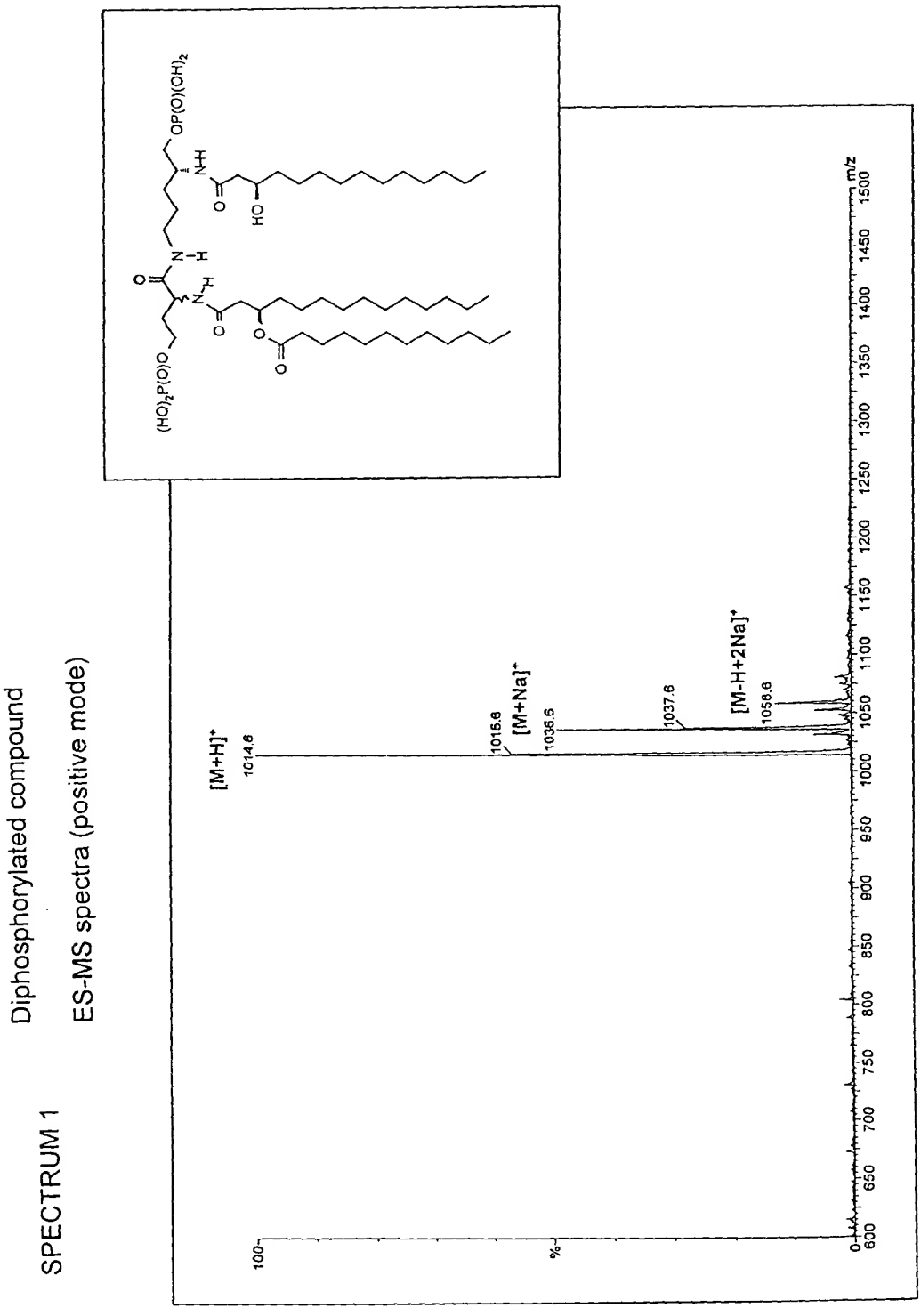

SPECTRUM 1
Diphosphorylated compound
ES-MS spectra (positive mode)
[M+H]+
1014.8
[M+Na]+
1015.6
1036.6
1037.6
[M-H+2Na]+
1058.6
100
%
0
600
650
700
750
800
850
900
950
1000
1050
1100
1150
1200
1250
1300
1350
1400
1450
1500
m/z
OP(O)(OH)2
(HO)2P(O)O
HO
Instrumentation: Micromass Quatro II (Z-spray), triple stage quadrupole

FIGURE 40

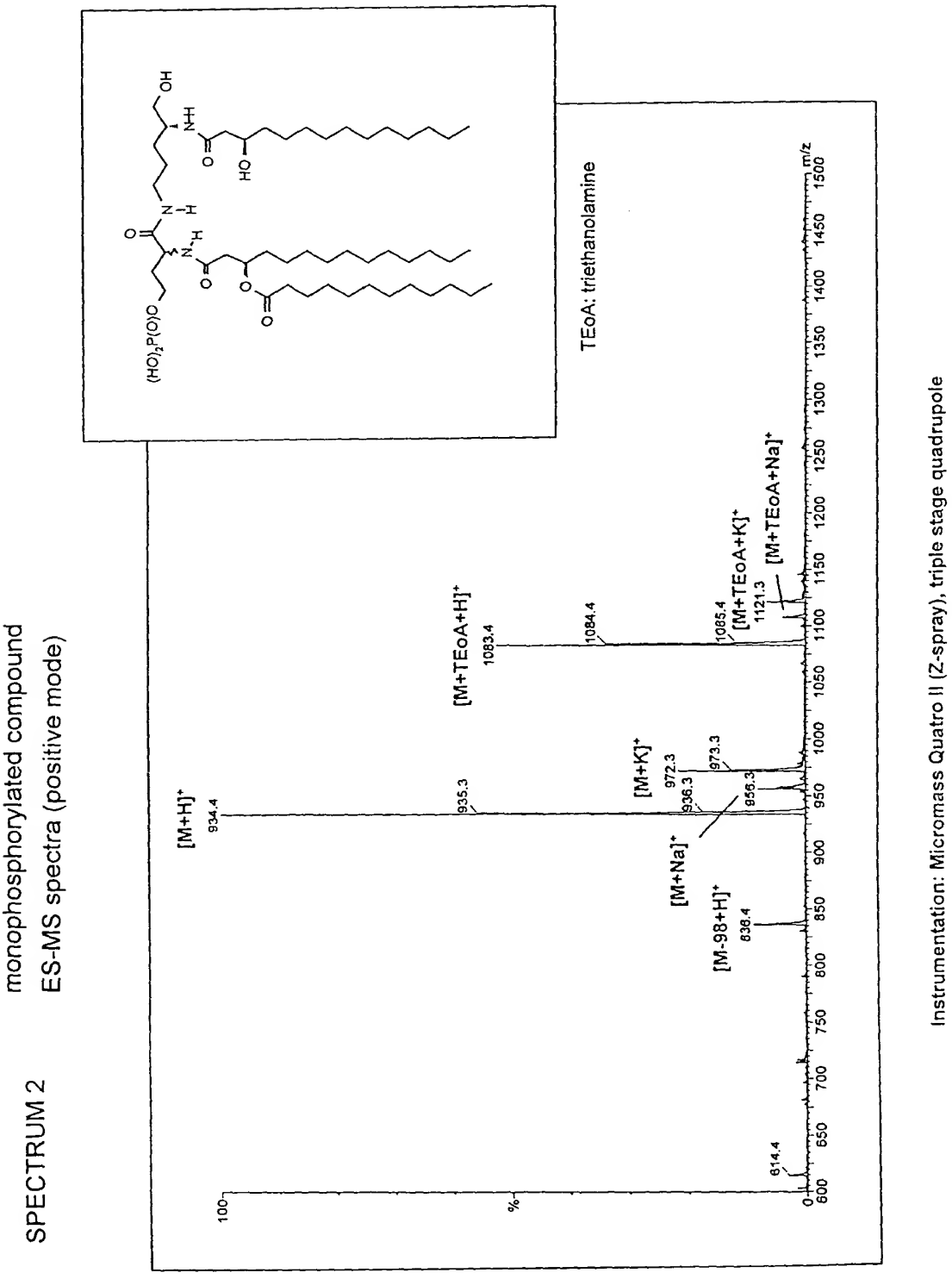
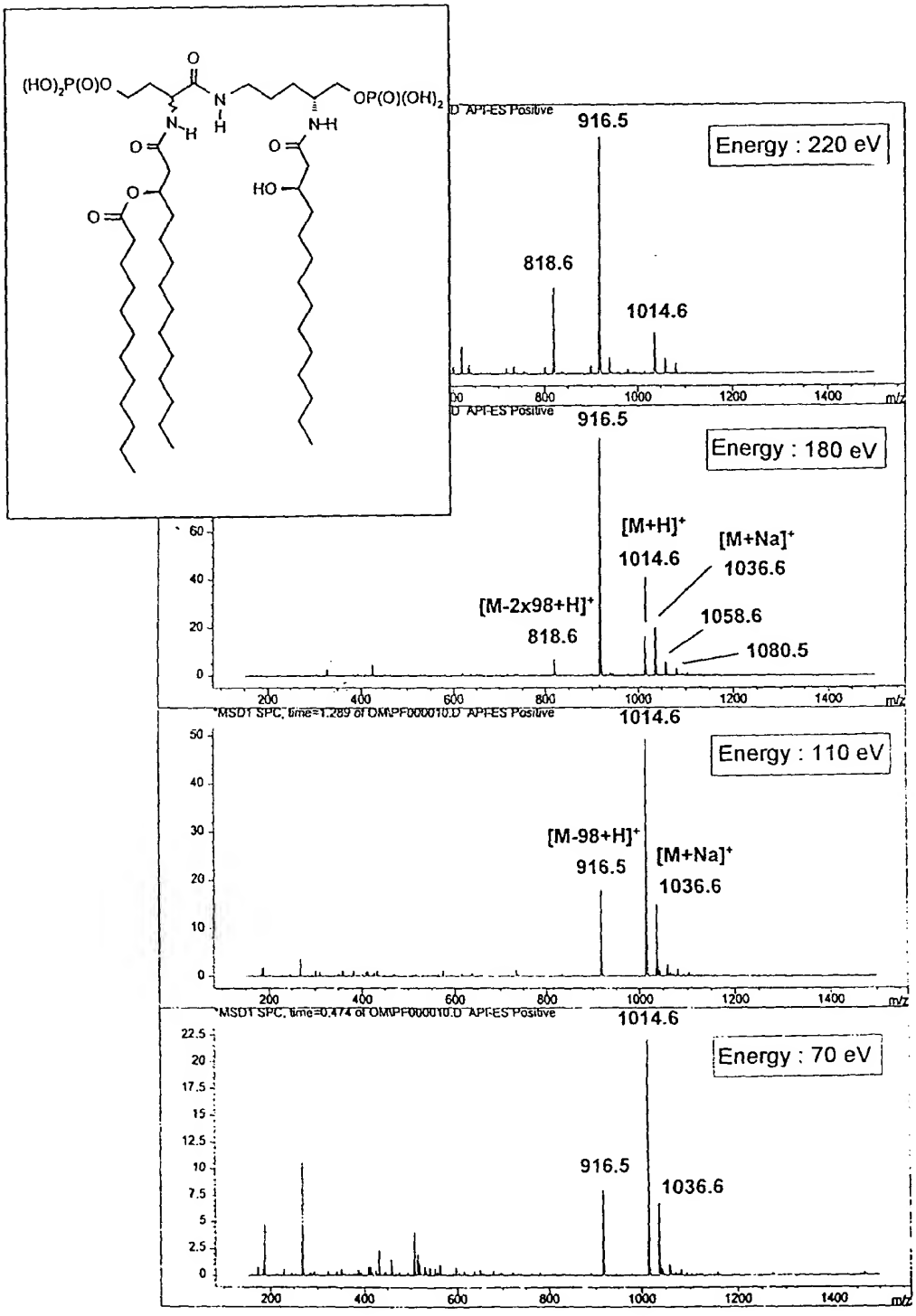

SPECTRUM 2
monophosphorylated compound
ES-MS spectra (positive mode)
TEoA: triethanolamine
[M+H]+
934.4
[M+TEoA+H]+
1083.4
[M+K]+
972.3
[M+Na]+
956.3
[M-98+H]+
838.4
[M+TEoA+K]+
1121.3
[M+TEoA+Na]+
614.4
100
%
0
600
650
700
750
800
850
900
950
1000
1050
1100
1150
1200
1250
1300
1350
1400
1450
1500
m/z
Instrumentation: Micromass Quatro II (Z-spray), triple stage quadrupole

FIGURE 41

SPECTRUM 3

Diphosphorylated compound

ES-MS spectra (positive mode fragmentation)



Instrumentation: Hewlett-Packard MSD, singl quadrupol

FIGURE 42

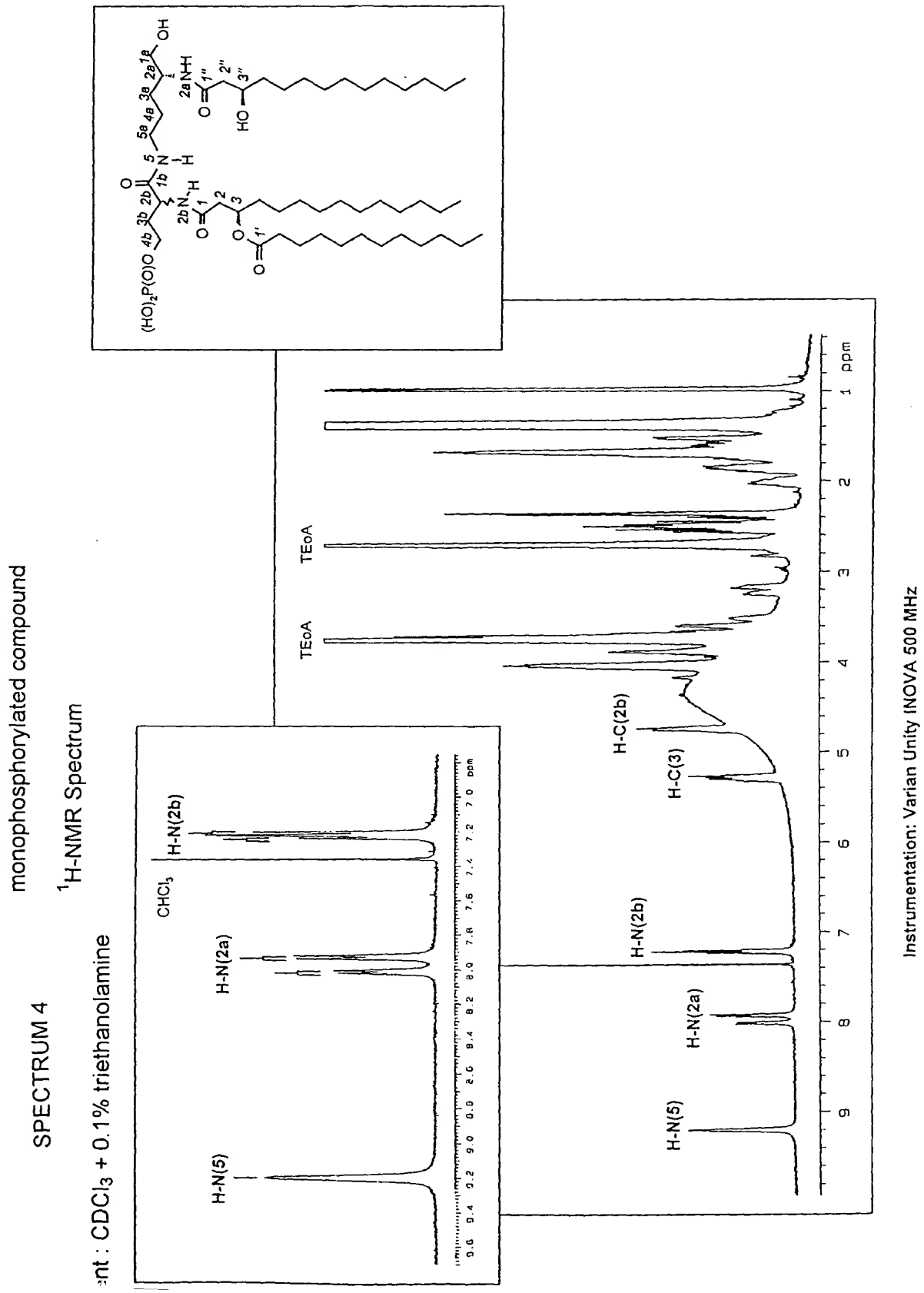

SPECTRUM 4
monophosphorylated compound
^{1}H-NMR Spectrum
nt : $CDCl_3$ + 0.1% triethanolamine
$(HO)_2P(O)O$
CHCl$_3$
H-N(5)
H-N(2a)
H-N(2b)
TEoA
TEoA
H-C(2b)
H-C(3)
H-N(2b)
H-N(2a)
H-N(5)
ppm
Instrumentation: Varian Unity INOVA 500 MHz

FIGURE 43

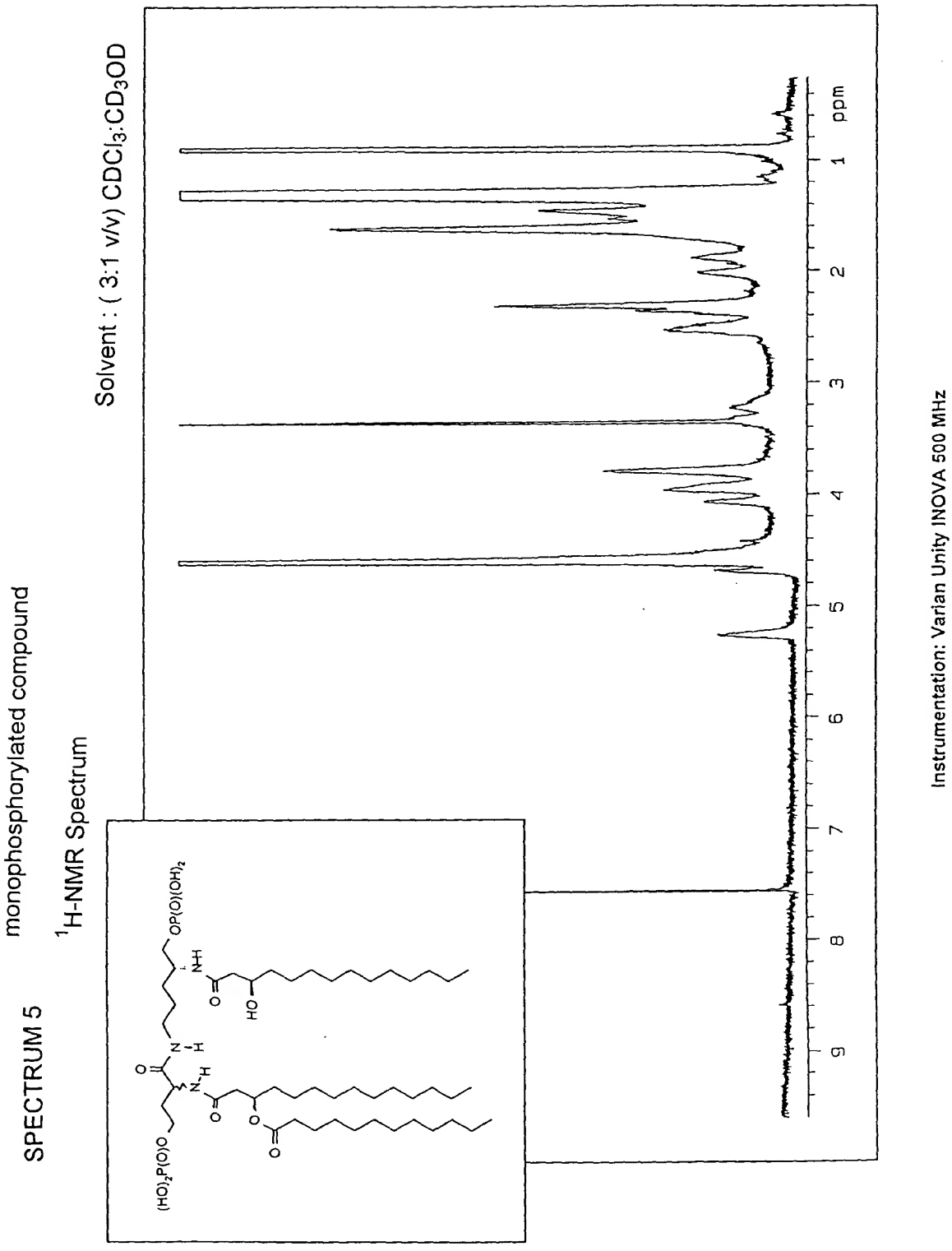

SPECTRUM 5
monophosphorylated compound
^{1}H-NMR Spectrum
Solvent : (3:1 v/v) $CDCl_3$:CD_3OD
ppm
Instrumentation: Varian Unity INOVA 500 MHz

FIGURE 44

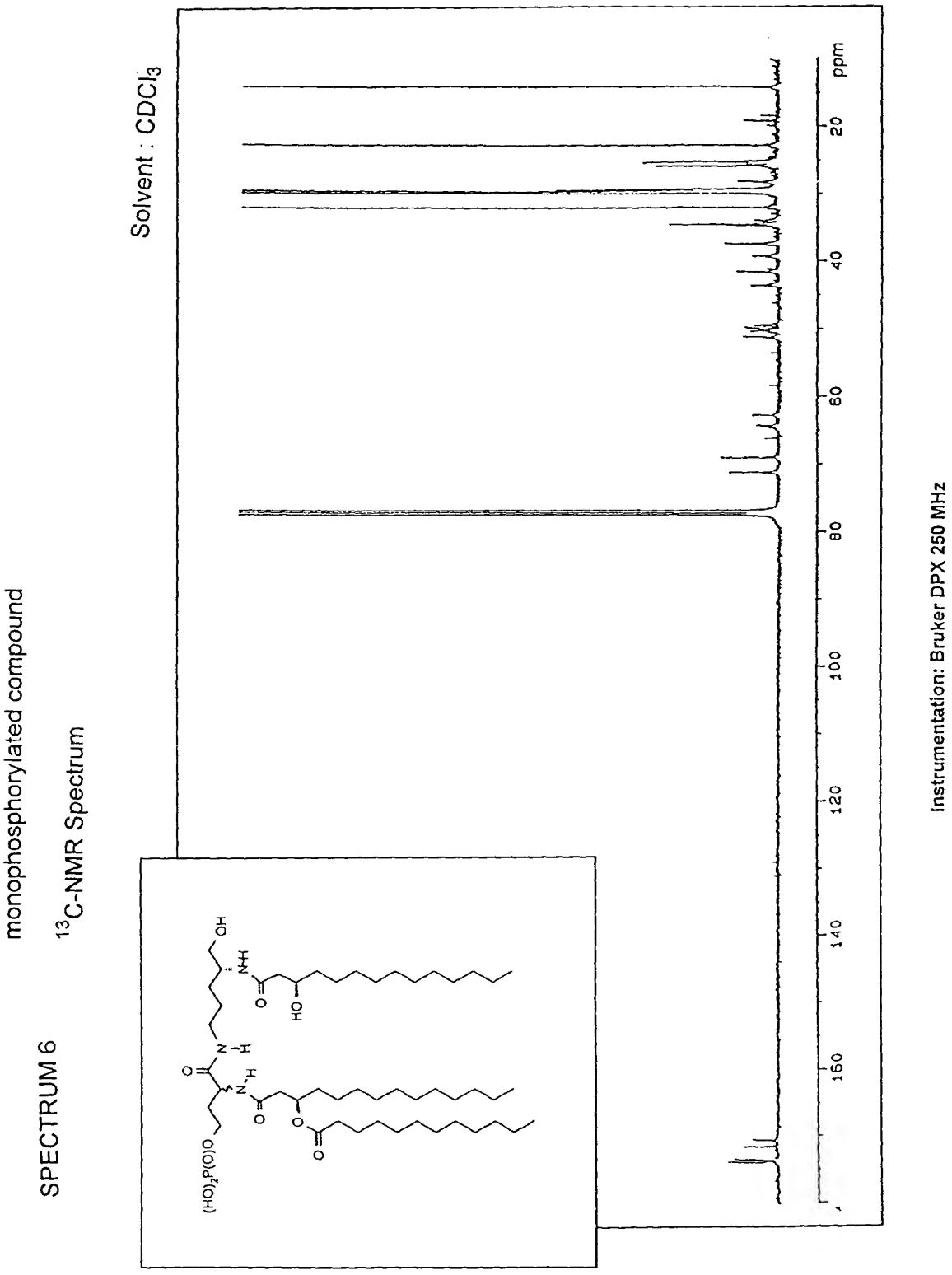

SPECTRUM 6
monophosphorylated compound
^{13}C-NMR Spectrum
Solvent : $CDCl_3$
ppm
20
40
60
80
100
120
140
160
Instrumentation: Bruker DPX 250 MHz

FIGURE 45

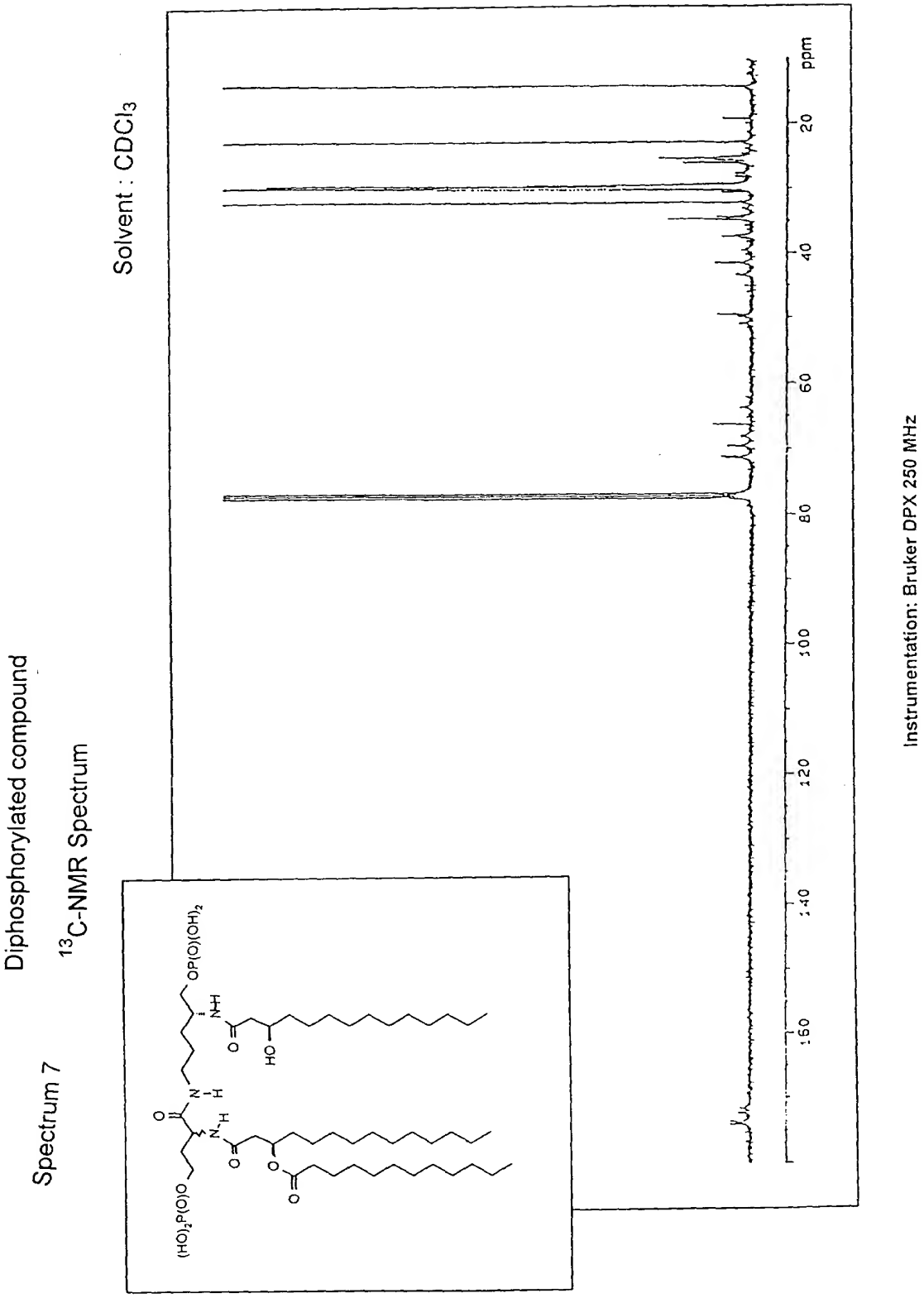
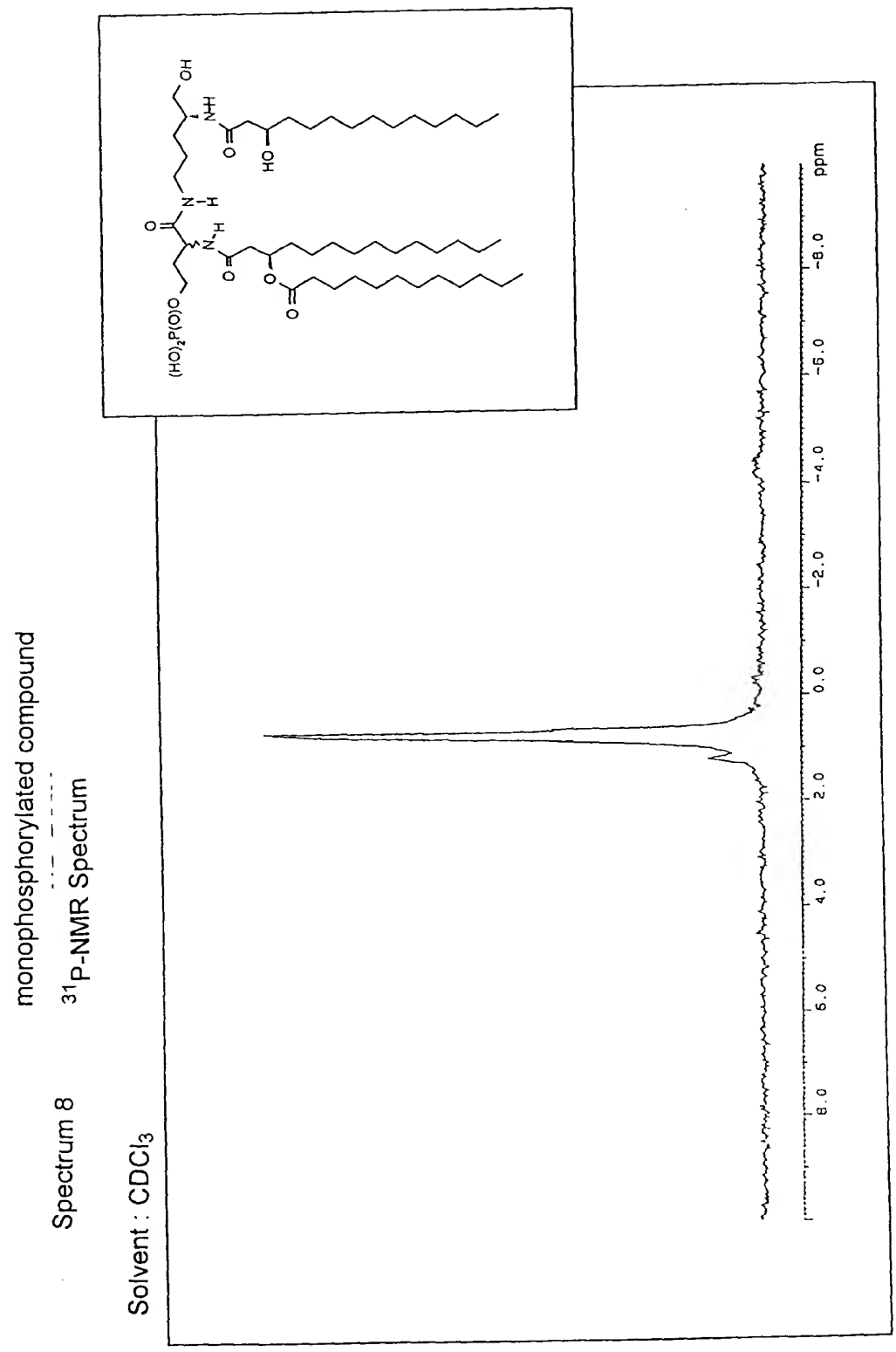
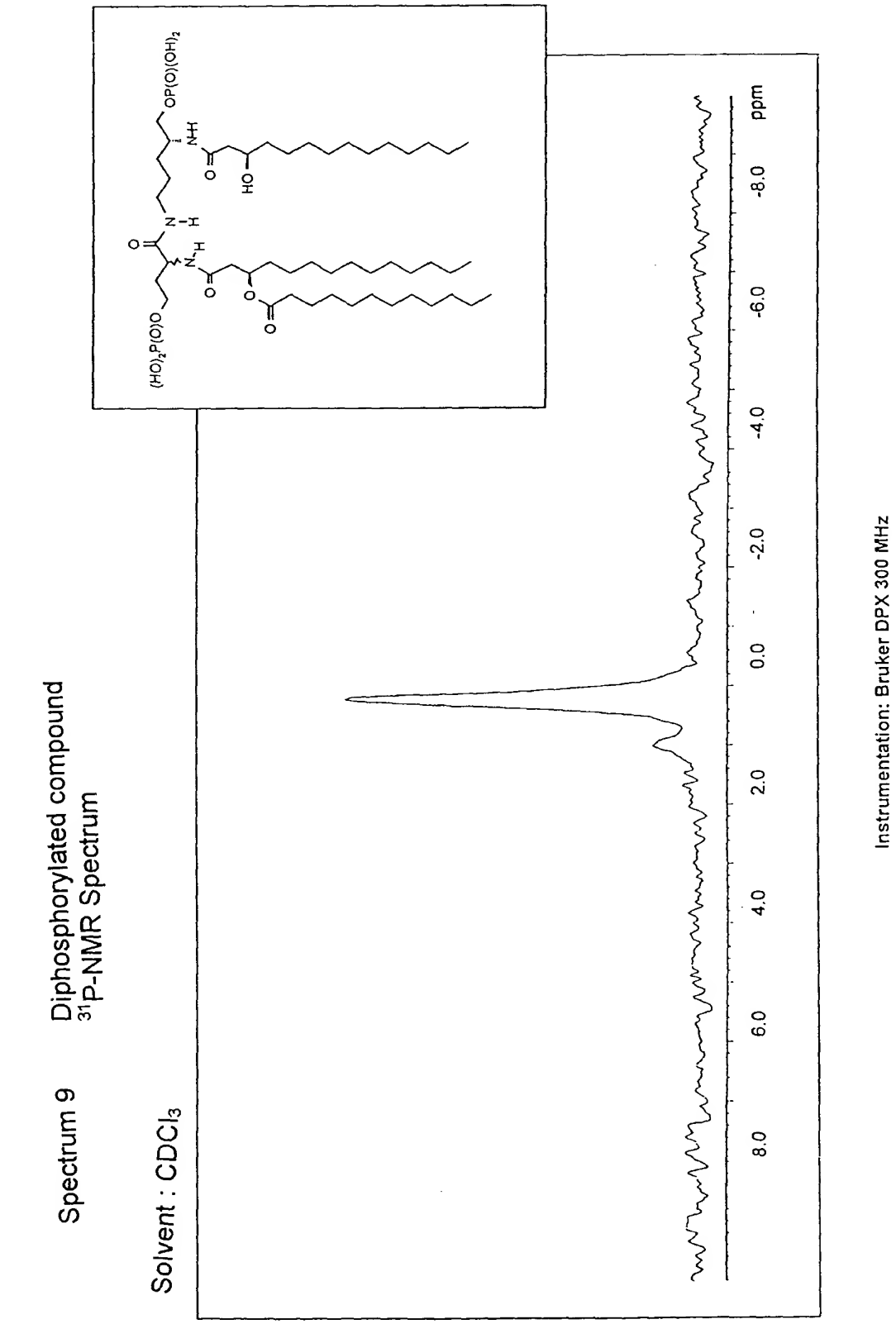

Spectrum 7
Diphosphorylated compound
^{13}C-NMR Spectrum
Solvent : $CDCl_3$
ppm
20
40
60
80
100
120
140
160
$OP(O)(OH)_2$
$(HO)_2P(O)O$
HO
Instrumentation: Bruker DPX 250 MHz

FIGURE 46



Instrumentation: Bruker DPX 300 MHz

FIGURE 47


Spectrum 9
Diphosphorylated compound
^{31}P-NMR Spectrum
Solvent : $CDCl_3$
8.0
6.0
4.0
2.0
0.0
-2.0
-4.0
-6.0
-8.0
ppm
Instrumentation: Bruker DPX 300 MHz